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Schuurmans, J. (2006). *Anxiety in late life: Moving toward a tailored treatment*. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam]. Partners Ipskamp.

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Anxiety in late life
Moving toward a tailored treatment

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The research project described in this thesis was funded by a research grant from the Dutch Health Research and Development Council, project number 940-33-036

Financial support for the printing of this thesis has been kindly provided by A.J. Schuurmans and GGZ Buitendamstel.

Illustrations: Bach Schuurmans

Cover design: Willem Mol willem.mol@quicknet.nl

Printed by: Print Partners Ipskamp B. V., Enschede, NL

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VRIJE UNIVERSITEIT

Anxiety in late life Moving toward a tailored treatment

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. T. Sminia,
in het openbaar te verdedigen
ten overstaan van de promotiecomissie
van de faculteit der Geneeskunde
op woensdag 18 januari 2006 om 15.45 uur
in de aula van de universiteit,
De Boelelaan 1105

door

Josien Schuurmans

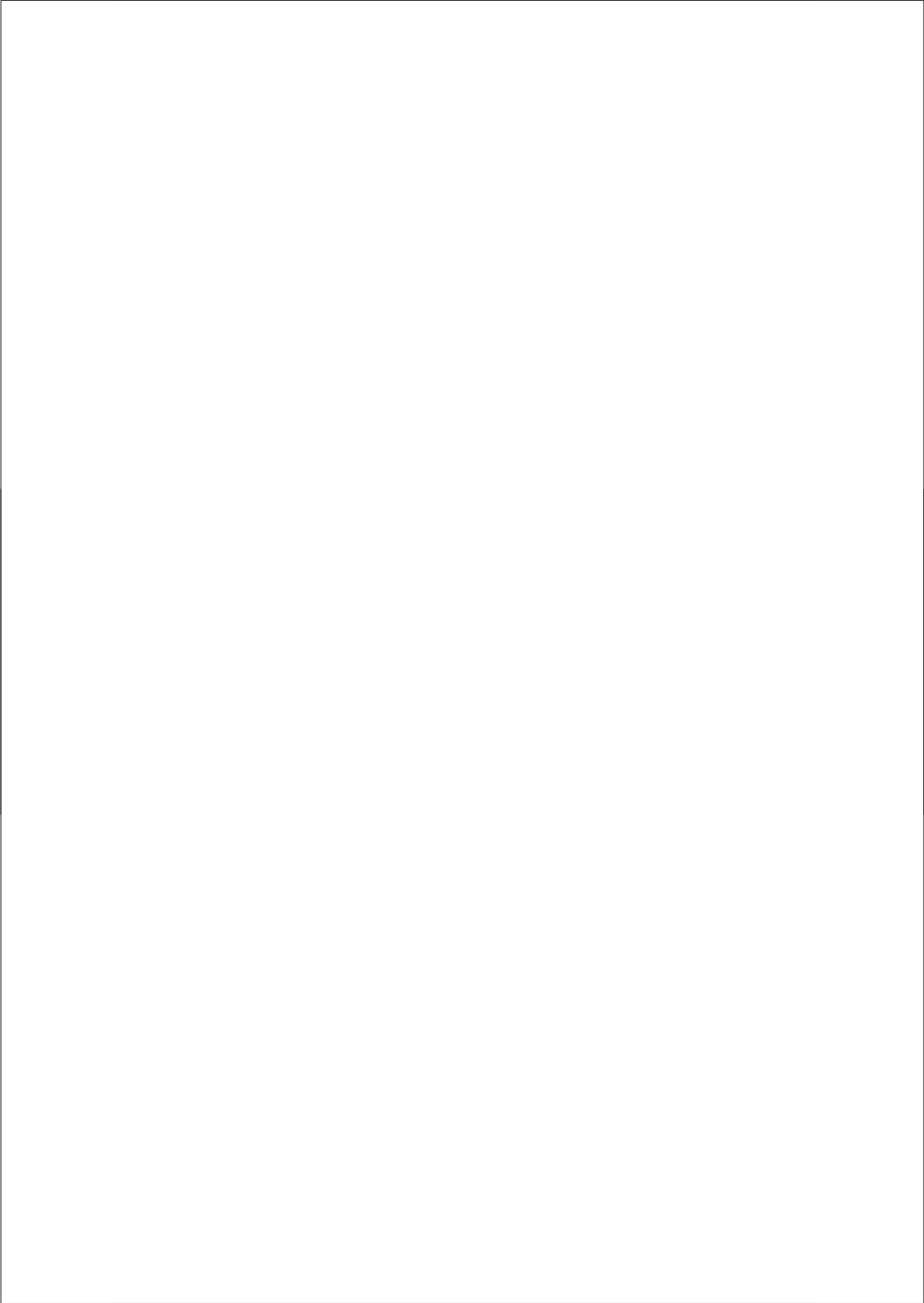
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promotoren: prof.dr. R. van Dyck
 prof.dr. P.M.G. Emmelkamp
copromotor: dr. H.C. Comijs

Voor (O)pa

‘ Kom, vul de glazen en denk langer niet
eraan hoe snel de onhoudbre tijd ontvlucht
Gisteren is dood, morgen nog niet geboren
Wat zou ‘t als ons vandaag genieten liet’

J.C. Bloem



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Chapter 1



General Introduction.

Late-life anxiety: Fact and fiction

This chapter is partly based on:

Schuurmans, J. & Weijnen, I. J. C. (2003). [Angststoornissen bij ouderen]: Anxiety disorders in older adults. In A. Bak, W. T. M. Berlo & J. J. L. Derksen (Eds.), *Handboek Klinische Psychologie* (22 ed., pp. 1-26). Houten: Bohn Stafleu van Loghum.

Preface

Until recently, the concept of anxiety in late life has been disregarded, both in clinical practice and in the scientific community. This disregard is still often thought to be justified by the fact that older adults with anxiety disorders rarely present themselves to mental health care settings. In fact, a recent study in the Netherlands revealed that only a very small percentage of older adults (aged 55 years and over) with an anxiety disorder were in contact with a community mental health care centre (3.8%) or a psychiatrist (2.6%) (de Beurs et al., 1999). In light of these circumstances, it is understandable that clinicians and researchers alike hold that anxiety is not very prevalent in late life. Other frequently voiced notions about late-life anxiety include the idea that depression is much more prevalent in late life, as well as the conviction that 'pure' anxiety disorders are hardly ever present in older adults and that anxiety in late life is almost exclusively a secondary by-product of a depressive disorder or a prelude to dementia. In recent years, all these assumptions have been refuted by epidemiological research, which will be discussed in the following paragraph.

Prevalence and comorbidity of anxiety in late life

Estimated prevalence rates of late life anxiety disorders in recent epidemiological studies center around 10% (Beekman et al., 1998; Flint, 1994), which is not very different from the estimated prevalence of 12.4% found in mixed-age populations

(18-65 years old; Bijl, Ravelli & van Zessen, 1998). Anxiety disorders are even found to be more prevalent in late life than depression (1.7%), dysthymia (3-5%) (Beekman & Heeren, 2001) and dementia (3-7%; (Verhey & Kat, 2001)). In contrast to the common clinical notion that anxiety in late life is either comorbid to depression or a symptom of mixed anxiety-depression, most older adults (74%) with an anxiety disorder do not suffer from a comorbid depression whilst depression without comorbid anxiety is much less common in late life (Beekman et al., 2000). Furthermore, mixed anxiety-depression is less prevalent in late life than either major depression or anxiety disorders (Schoevers, Beekman, Deeg, Jonker & van Tilburg, 2003). Although symptoms of agitation and anxiety frequently accompany dementia, the prevalence of anxiety disorders among persons with dementia is comparable to the prevalence of anxiety disorders in the general population of older adults (Chemerinski, Petracca, Manes, Leiguarda & Starkstein, 1998). In a report on the comorbidity of anxiety disorders in older adults in the Netherlands, no significant association was found between the presence of an anxiety disorder and the presence of cognitive impairment (van Balkom et al., 2000). When trying to establish whether anxiety could possibly be a prelude to dementia, it is important to closely investigate the etiology of anxiety symptoms. Most anxiety disorders in late life have an onset in early or middle adulthood (Flint, 1994), which makes it highly unlikely that there is any connection with dementia.

Recognition and presentation of late-life anxiety disorders

In light of the high prevalence of anxiety in late life, it is puzzling that only a very small minority of older adults that are referred to mental health care settings are diagnosed with an anxiety disorder. Several factors may contribute to the fact that anxiety disorders are not easily identified in older adults.

First of all, older adults may be more inclined to verbalize psychological symptoms in somatic terms (Godderis, van de Ven & Wils, 1992). Psychological terminology is less familiar to older adults and anxiety symptoms are often described in terms of physical illness: e.g. "I feel sick". Furthermore, older adults with anxiety are most

frequently seen in a primary care setting rather than in a specialized mental health care setting, and the general practitioner is inclined to give high priority to somatic complaints in an older adult. Justifiably so, since older adults have a greatly increased risk of somatic illness (Haley, 1996), but in the process of excluding a somatic cause, the possibility of an anxiety disorder is often overlooked.

Secondly, the current generation of older adults is probably more reluctant to share their personal problems with other people, as they were raised to solve their own problems and not to involve other people in private matters (Weijnen, 2001). Additionally, clinical experience tells us that older adults are more inclined to think of anxiety symptoms as a personality trait that can not be altered or cured, especially when their symptoms have an onset in childhood or early adulthood. For older adults who have been struggling with anxiety symptoms for decades and who have never been (adequately) treated, it is not very logical to suddenly start demanding treatment for their ailment, particularly when they have the impression that such a treatment does not exist. Therefore, it does not come as a surprise that anxiety symptoms are rarely spontaneously reported by older adults.

Anxiety in late life may also go unnoticed through effective avoidance behavior. It is probably easier for older adults to avoid certain activities since they have less obligations than younger adults and society readily accepts the fact that older adults are incapable of physical exercise or of doing their own shopping (Weijnen & de Beurs, 2001). People surrounding an older individual (e.g. children, neighbors) are probably more prone to relieve the older adult of the burden of certain tasks than they would be when confronted with a younger adult with similar problems. Although well intended, this helpfulness may contribute to the onset and persistence of avoidance behavior and the camouflaging of anxiety symptoms.

Another related factor contributing to the lack of appropriate identification and referral of anxiety in late life lies within the (mental) health care profession rather than within the anxious older adult. Ageism (Lindesay, 1991) is probably involved in the fact that anxiety and avoidance behavior in late life are often interpreted as 'normal' or 'realistic' (Fuentes & Cox, 2000) and, therefore, deemed untreatable. For

example, when an older person's mobility is affected by arthritis or other age-related ailments, or when an older person trips and falls in the street, it is often considered an appropriate response for that person to be too anxious to leave the house or travel by bus, train or tram. On the same note, when we are confronted with an older person who obsesses over the possibility of becoming seriously ill or cognitively impaired, our own fears of what might happen when we grow old may hinder the correct appraisal of such obsessive thoughts as symptoms of an anxiety disorder.

Furthermore, the phenomenology of anxiety in late life may be different from anxiety in early adulthood: older adults may fear different stimuli or situations or may have a different reason for fearing certain stimuli or situations than younger adults (Schuurmans & Weijnen, 2003). Current diagnostic instruments and the DSM-IV classification system may not be cut out to identify late-life anxiety disorders.

In the next paragraph, an account is given of the prevalence of different anxiety disorders and of the way they may present themselves in late life.

Prevalence and clinical presentation of specific anxiety disorders in late life

In diagnosing anxiety disorders in late life it is sensible to discriminate between early and late onset of anxiety (Flint, 1997; Sheikh & Salzman, 1995b). In early onset anxiety (before the age of 60), the clinical presentation may be similar between older and younger adults. In late onset anxiety (at or after the age of 60), it is plausible that more age-related features are present. Late-onset anxiety is not as rare as current clinical lore holds. In fact, it is present in 30 to 40% of late-life anxiety disorders (Le Roux, Gatz & Wetherell, 2005; Flint, 1994).

Table 1. The prevalence of anxiety disorders in mixed-age populations (<65) and older adults (>55) in the Netherlands

Diagnosis	Mixed-age (<65)	Older adults (55+)
All anxiety disorders	12.4%	10.2%
Panic disorder	2.2%	1.0%
Agoraphobia	1.6%	3.1%
Specific phobia	7.1%	
Social phobia	4.8%	
Generalized anxiety disorder	1.2%	7.3%
Obsessive-compulsive disorder	0.9%	0.6%

The present thesis focuses on four specific anxiety disorders: generalized anxiety disorder, agoraphobia, social phobia and panic disorder, as these are generally regarded to be most prevalent in late life.

Generalized anxiety disorder (GAD)

GAD appears to be the most prevalent anxiety disorder in late life with an estimated prevalence rate in the Netherlands of 7.3% (see table 1; Beekman et al., 1998), which is almost six times as high as the estimated prevalence of GAD in younger adults (1.2%; Bijl, van Zessen & Ravelli, 1997). Early onset GAD shows great resemblance to the concept of 'trait anxiety'. Late-onset GAD is presumably triggered by a major life event, such as retirement, the death of one's partner or the establishment of the presence of a physical illness.

In part, the focus of worry symptoms seems to shift with age. Worries about health-related issues peak in older adults, while younger adults tend to worry more about their family and finances (Person & Berkovec, 1995). Fear of crime increases strongly with age, even though older adults are not victimized more often than younger adults (Clarke & Lewis, 1982). Presumably, this may be attributed to the sense that one's capacity to defend oneself is diminished (Godderis et al., 1992).

Agoraphobia

Data on the prevalence of agoraphobia in late life are scarce. However, the estimated prevalence of all phobic disorders combined (agoraphobia, social phobia and specific phobia) is 3.1% in older adults in the Netherlands (Beekman et al., 1998); see table 1). One study found a prevalence rate of 1.4% for agoraphobia in older adults (Weissman et al., 1985), which would mean that agoraphobia is the second most prevalent anxiety disorder in late life. Although agoraphobia in the classical sense, with a history of panic attacks or panic symptoms, is not uncommon in older adults, one may also find a completely different etiology of this disorder in late life. Physical limitations or an accident are often found to be a trigger for late-onset agoraphobia. Especially the fear of falling appears to be common in late life. This fear can be so incapacitating that it fits the criteria for an anxiety disorder: the so-called 'fall phobia' (Spano & Forstl, 1992). Health care professionals tend to regard this fear as realistic and therefore, not pathological. However, although a fall may be a valid reason for taking the necessary safety precautions, it does not imply that one should never leave the house without a chaperone. Incontinence, present to some extent in 60 percent of older adults, can also contribute to the onset of agoraphobic symptoms in late life. In this case, unfamiliar or crowded places are avoided because a toilet may not be readily available.

Social phobia

Among people under 65, social phobia is the second most prevalent anxiety disorder. Social phobia appears to be less prevalent in older adults (Gretarsdottir, Woodruff-Borden, Meeks & Depp, 2004), although exact figures are unfortunately not available. However, social phobia may take on a different form in late life, which might complicate the correct identification of this disorder in older adults.

With increasing age, the focus of social anxiety seems to shift from the fear of public speaking to the fear of eating, drinking and writing in public (Sheikh et al., 1995), the feared consequence being that other people will see you spill or tremble. In these cases, the adaptation to a life with dentures, paralytic symptoms after a

cerebrovascular accident, an age-related tremor or Parkinson's disease contribute to the etiology of a social phobia in late life. Even the fear of developing dementia can be interpreted as a form of social phobia when related avoidance behavior is very incapacitating. Older adults may become fearful of being perceived by others as someone suffering from dementia in reaction to seemingly small incidents, such as forgetting someone's name or not being able to find one's keys. In company, people may become fearful that others will notice their forgetfulness and as a consequence, social situations may be avoided. Anxiety and tension may in turn lead to an aggravation of forgetfulness through a lack of concentration, which can be interpreted as a confirmation of the alleged dementia, not only by the older adult in question, but also by relatives and acquaintances. It is important to distinguish this phobia from legitimate memory complaints in older adults. In cross-sectional studies, evidence has been found that memory complaints are significantly but weakly associated with memory impairment (Jonker, Geerlings & Schmand, 2000). Longitudinal studies suggest that memory complaints reflect a greater risk for dementia or cognitive decline, but only in those older adults with mild cognitive impairment at baseline. In highly educated older adults, subjective memory complaints may be associated with future cognitive decline or dementia even without the presence of such mild cognitive impairment at baseline (Jonker et al., 2000). However, the evidence for the association between memory complaints and cognitive decline is limited and equivocal. Furthermore, it is important to keep in mind that the available evidence does not imply that the majority of older adults who complain of memory problems will eventually develop dementia.

Incontinence may also be a factor in the etiology of late-onset social phobia, in which case company is avoided because one fears that their incontinence will lead to embarrassment.

Panic disorder

Panic disorder, as described in the DSM-IV, (American Psychiatric Association, 1994), is less prevalent in late life than in early or middle adulthood. Its prevalence is estimated at 0.1-1.0% in people aged 55 years and over (Beekman et al., 1998; Flint, 1994; Regier et al., 1988) versus 2.2% in younger adults (Bijl et al., 1998). Panic symptoms in older adults often do not fit the description of recurrent panic attacks, because the symptoms do not follow a short and overwhelming pattern, but instead tend to show a more chronic and less “violent” course. This phenomenon is possibly caused by normal age-related differences in bio-psychosocial variables that contribute to the severity of panic symptoms (Sheikh, Swales, Carlson & Lindley, 2004; Flint et al., 1998). Effective avoidance behavior may also contribute to the absence of panic attacks. For example, if an older person never goes to the supermarket at times when it is fairly crowded, panic attacks are easily avoided. Late-onset panic disorder has been found to be associated with less severe and fewer symptoms than early-onset panic disorder (Seguí et al., 2000; Sheikh, King & Barr Taylor, 1991).

The burden of anxiety in late life

In the previous section of this chapter, the common belief that anxiety disorders are rare in late life has been refuted by evidence from epidemiological studies, and explanations for the lack of appropriate identification of anxiety disorders in late life have been put forward. However, current clinical opinion also proclaims that anxiety in late life is not very serious or incapacitating. In fact, recent studies show that the opposite is true: late-life anxiety has been proven to be equally disabling as late-life depression (de Beurs et al., 1999). The use of somatic health care services (visits to the general practitioner, medical specialists, hospital admissions) is increased in anxious older adults, while the appropriate use of mental health care services is low (de Beurs et al., 1999). Furthermore, findings from recent studies suggest that anxiety is associated with an increased mortality rate in male older adults (van Hout et al., 2004) and in frail or chronically ill older adults (Crockett, Cranston, Moss & Alpers, 2002; Strik, Denollet, Lousberg & Honig, 2003). In older adults who have suffered

from a myocardial infarction, anxiety has been found to be predictive of recurrent cardiac events and an increased use of health care services (Strik et al., 2003). Anxiety disorders have also been found to be more prevalent in chronically ill older adults (Kim, Braun & Kuni, 2001).

Data on the course and long-term outcome of anxiety in late life are nonexistent, but studies in mixed-age populations have shown that anxiety disorders that are not adequately treated tend to follow a chronic course (Angst & Vollrath, 1991).

Feasibility and effectiveness of treatment for late-life anxiety disorders

Psychological interventions

Despite the prevalence and impact of anxiety in late life, the belief that it is not sensible or feasible to undertake a psychological intervention in anxious older adults is still common in general practitioners and mental health care professionals. This belief dates back to the early days of psychoanalytic theory; Freud proclaimed that psychotherapy would not be feasible for an older individual (Jacobs, 1994), because a person's psychological flexibility was supposed to diminish through the years and the amount of material that had to be addressed in the analysis would have become too expansive.

In response to this reluctance to treat anxious older adults, a counter movement has been set in motion that proclaims that the same treatments that have been found to be effective in younger adults, can and should be applied to older adults. Research efforts that stem from this counter movement, have focused on establishing the effectiveness of cognitive behavioral therapy (CBT) for late-life anxiety, as empirical evidence suggests that CBT is the most effective form of psychotherapy for anxiety disorders in mixed-age populations (Emmelkamp, 2004).

In the last decade, several studies have been published that provide modest support for the effectiveness of CBT in anxious older adults (Stanley et al., 2003; Mohlman et

al., 2003; Wetherell, Gatz & Craske, 2003; Barrowclough et al., 2001; Stanley, Beck & Glassco, 1996). One of these studies (Wetherell et al., 2003) compared the relative effectiveness of CBT to a discussion group focused on worry-provoking topics in older adults with a generalized anxiety disorder. Both treatment conditions proved to be superior to a wait list control group, but there was only limited evidence of the superiority of CBT over the discussion group. In another recent study (Stanley et al., 2003), CBT was compared to a minimal contact control group in older adults with a generalized anxiety disorder (GAD). CBT was found to be superior to the control group, with 45% of participants in the CBT group showing significant improvement, versus 8% in the control group. The effect remained fairly constant over a follow-up period of one year. Only one randomized treatment study included older adults with a wider range of anxiety disorders, rather than focusing solely on GAD (Barrowclough et al., 2001). In this study CBT was compared to supportive therapy for the treatment of older adults with panic disorder, social phobia, GAD and anxiety disorder not otherwise specified (ADNOS). Both CBT and supportive therapy proved to be effective, with CBT participants showing greater improvement on anxiety measures. Also, response rates in the CBT group were higher; 71% of participants who received CBT were identified as treatment responders, versus 39% of participants who received supportive therapy. These findings are in disagreement with findings from an earlier study by Stanley et al. (1996) in which response rates for supportive therapy were higher than for CBT (54% vs. 28%). Both studies lacked a control group, although a six-week baseline phase was used in the study by Barrowclough et al. (2001) in order to ensure the stability of anxiety symptoms.

Although the treatment studies described here provide some support for the effectiveness of CBT for late-life anxiety disorders, the superiority of CBT over other modes of treatment for this particular group has not been firmly established and effect sizes in these studies tend to be smaller than effect sizes found in similar studies of mixed-age populations (Mohlman, 2004). Also, most treatment studies of late-life anxiety disorders are characterized by relatively high dropout rates (Stanley et al., 2003; Wetherell et al., 2003; Stanley et al., 1996) when compared to similar studies in younger adults (Gould, Safren, Washington & Otto, 2004). This is an

important factor to take into account when evaluating the effectiveness of CBT for late-life anxiety, since dropout can be regarded as a type of treatment failure (Emmelkamp & van der Hout, 1983) and may lead to a bias of research findings; dropouts have been found to differ from those who complete treatment in several studies (e.g. Issakidis & Andrews, 2004; Cuijpers, 1998). Finally, since older adults do not readily apply for referral to a mental health care setting, recruitment for late-life anxiety treatment studies is primarily accomplished through media announcements (Akkerman et al., 2001; Wetherell & Gatz, 2001). Media recruitment of participants also carries the risk of biased research findings, as has been put forward by several publications on media recruitment in mixed-age populations (Rapaport et al., 1996; Aronson, 1987; Krupnick, Shea & Elkin, 1986).

It is often stated that cognitive behavioral therapy should be modified to accommodate older adults. This is why CBT in studies with older adults is often provided in a group format (e.g. Stanley et al., 2003; Wetherell et al., 2003), rather than the individual format in which it is usually provided to younger adults. The rationale behind this approach is that older adults may be more socially isolated than younger adults and will benefit more from treatment in a group (Stanley et al., 2003). Other recommended modifications for older adults involve a greater emphasis on psycho-education, increasing the patient's motivation and repeating the explanation of new coping strategies. It is often suggested that psycho-education is more important in older adults, because the present older cohort may have unrealistic views of what psychotherapy entails and may also have more trouble identifying, and talking about, psychological problems. More emphasis on increasing the motivation of patients is presumed to be needed, because people have often been living with their symptoms for decades and are reluctant to believe that recovery is possible. Treatment studies described here all claim to have incorporated some or all of these modifications in their CBT protocols, but no systematic study has been performed to establish if, and which modifications are necessary to improve the effectiveness of CBT for late-life anxiety disorders. Recently, a pilot study has been published, comparing standard CBT with an adapted CBT protocol for older adults in the treatment of GAD, that provides some indication that the adapted protocol

might lead to better results (Mohlman et al., 2003). Adaptations involved the use of learning and memory aids, more attention to the (repeated) explanation of the rationale of treatment and weekly calls from the therapist to help participants with any problems they might have encountered in doing the homework assignments.

In conclusion, although CBT appears to be effective for the treatment of anxiety in older adults, the evidence is limited and equivocal. Because CBT in late-life anxiety treatment studies is often provided in a group format it is difficult to distinguish group effects from treatment-specific effects. Also, because most studies have focused on the treatment of GAD, no inferences can be made on the effectiveness of CBT for other anxiety disorders in older adults. Surprisingly, none of the aforementioned studies included participants with agoraphobia without a history of panic disorder, while this may well be one of the most common anxiety disorders in older adults (Beekman et al., 1998).

Pharmacological interventions

The most common form of treatment for late-life anxiety today is the prescription of benzodiazepines. As many as 25% of older adults with an anxiety disorder in the Netherlands were found to use a benzodiazepine (de Beurs et al., 1999). In fact, benzodiazepines are the most commonly prescribed psychotropic drug in older adults, regardless of psychiatric diagnosis (Kirby et al., 1999). This is a troubling phenomenon, since a long-term use of benzodiazepines is associated with serious adverse effects, especially in older adults, such as a heightened risk of accidents and falls, a heightened risk of cognitive impairment and the development of tolerance and addiction (Broekhoven et al., 2002; Kan et al., 1997).

In trying to reverse the wide distribution of benzodiazepines among anxious older adults, several authors (Nordhus & Pallesen, 2003; Hersen & van Hasselt, 1992) have warned against pharmacological treatments of late-life anxiety in general, because even the prescription of safer psychotropic drugs, such as selective serotonin reuptake inhibitors (SSRIs) might be problematic in older adults. Due to a slower

metabolism in older adults, especially in those with one or more chronic diseases, there is a greater chance of adverse side-effects. Furthermore, older adults often already use a lot of different medications, increasing the chance of negative interactions. Although these are valid arguments, they do not provide sufficient basis to completely discard any kind of pharmacological approach. In fact, data on the prescription of SSRIs for late-life depression indicate similar effectiveness and tolerability of these drugs in older adults as in younger populations (Bourin, 2003; Mottram, Aswhorth & Abou-Saleh, 2003; Schneider et al., 2003), even in the 'older old' (aged 75 years and up; Gildengers et al., 2002). Recently, the first randomized placebo-controlled trial of an SSRI (citalopram) for the treatment of late-life anxiety has been published, providing support for the efficacy of SSRIs for the management of anxiety in older adults (Lenze et al., 2005). However, the study sample was rather small (n=17 in the citalopram condition versus n=17 in the placebo group) and findings need to be replicated in a larger sample. Also, a recent pooled analysis of five randomized placebo-controlled trials of venlafaxine for generalized anxiety disorder in mixed-age populations suggested that venlafaxine is equally efficacious, safe and well tolerated in younger and older patients (Katz, Reynolds, Alexopoulos & Hackett, 2002).

How old is an 'older adult'?

It should be noted that in the available literature on late-life anxiety, the age that is used as a cut-off for defining 'late life' often differs between studies. In most studies, the cut-off used is 55, 60 or 65 years old. The Dutch ministry of Public Health, Well-being and Sports defines an older adult as someone aged 55 years or older. In the Netherlands, specific mental health care facilities for older adults usually define an older adult as someone aged 60 years and over. However, many of us may tend to have a higher age in mind to delineate late life.

Aims and outline of the present thesis

The present thesis attempts to contribute to the appropriate identification, prognosis and, especially, the effective treatment of late-life anxiety. We hypothesized that differences in the phenomenology of anxiety between older and younger adults might contribute to the lack of appropriate identification of anxiety disorders in late life. Therefore, we conducted a study in the general population that aimed to establish differences between the phenomenology of anxiety in older, younger and middle-aged adults. In this study, both common measures for anxiety and a new questionnaire designed to measure age-related worry symptoms in older adults are used in order to find cues for appropriate identification of anxiety in older adults. Findings from this study are described in chapter 2.

In order to establish whether anxiety disorders have a similar tendency to show a persistent long-term outcome in late life as has been established in younger populations (Angst et al., 1991), we studied the outcome of anxiety disorders and factors related to outcome in a cohort of anxious older adults in the Netherlands after a follow-up period of six years (chapter 3). This chapter also provides data on the use of mental health care facilities in order to establish whether efforts made in recent years to enhance appropriate referral have taken effect.

As described in a previous section of this chapter, late-life anxiety disorders are mostly treated with benzodiazepines. In an effort to find support for the effectiveness of more adequate interventions that are successfully applied to younger populations for the treatment of anxiety in late life, we performed the first randomized comparative trial of CBT versus an SSRI (sertraline) for anxiety disorders in older adults. Chapter 4 describes the main findings of the RCT, whilst chapter 5 deals with long-term outcome of CBT and sertraline at one-year follow-up and differential predictors for treatment effect, in order to establish what treatment might work best for whom. As attrition rates in treatment studies of late life anxiety are typically high and early termination of treatment can be regarded as a type of treatment failure (Emmelkamp et al., 1983), we also studied factors related to treatment dropout. Furthermore, we hypothesized that high attrition rates and the recruitment of

subjects through media announcements for treatment studies of late-life anxiety might be a source of bias for research findings. Therefore, chapter 6 describes an investigation of differences between treatment dropouts and completers and between recruited and clinically referred participants of our RCT. Finally, in chapter 7, findings from the studies described in the previous chapters are integrated and discussed.

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Chapter 2



The phenomenology of anxiety in older adults.

Abstract

Objective: Differences in the phenomenology of anxiety between older and younger adults may contribute to difficulties in the recognition and treatment of late-life anxiety. In order to examine differential aspects of late-life anxiety, young adults, middle-aged adults and older adults were compared with respect to differences in fear evoking stimuli (CS) and cognitive contents of anxiety (UCS). **Method:** Data were collected by means of a mail survey in a sample of 513 representative participants in the Netherlands, divided equally in three age groups of 18-44 years, 45-64 years and 65 years and over. Fear-evoking stimuli were measured with the Fear Survey Schedule (FSS). Cognitive contents were measured with the Worry Domains Questionnaire-Revised (WDQ-R) and a newly devised instrument, the Senior Anxiety Scale (SAS). ANCOVA's and post-hoc Bonferroni corrected t-tests were conducted on all total scores and subscale scores to test for differences between age groups. **Results:** Both middle-aged and older adults scored higher than young adults on the FSS, and older adults scored higher on the sex and aggression subscale than both middle-aged and young adults. The WDQ showed that older adults were less worried about finances than their younger counterparts. The SAS revealed a four-factor structure, which explained 54.7% of the total variance in scores. Older adults scored higher than young adults on two of the factors, one representing the fear of decline of physical and mental health and one representing the fear of life-threatening situations. **Conclusion:** The SAS appeared to be a valid instrument for measuring age-related cognitive content of anxiety in older adults. Older adults seem to be more worried about the decline of physical and mental health, death and criminal assault than their younger counterparts. Further development of measures of anxiety incorporating items relevant to the daily life of older adults is needed to firmly establish the phenomenological differences between anxiety in younger and older adults.

This chapter is a modified version of the following manuscript:

Weijnen, I.J.C., Schuurmans, J., Comijs, H.C., Emmelkamp, P.M.G., van Dyck, R. & van Hout, M.A. (*submitted*). Phenomenology of anxiety in older adults: a cue for better recognition?

Although several epidemiological studies (Flint, 1994a; Beekman et al., 1998b) have shown anxiety symptoms and anxiety disorders to be highly prevalent (10%) and disabling in older adults (de Beurs et al., 1999), clinicians in mental health care centers often attest to the fact that they are hardly ever confronted with anxious older adults. In fact, older adults seem to be underrepresented in clinical practice irrespective of psychopathology: only 2 to 5% of the patients in mental health care are 65 years or over (Stanley & Averill, 1999). This misrepresentation partly stems from problems with recognition of anxiety in older adults, leading to a lack of appropriate referral and treatment of anxious older adults (Alwahhabi, 2003; Stanley, 2002; Sheikh & Salzman, 1995; Lindesay, 1991).

Most explanations that have been put forward for the discrepancy between prevalence rates of late-life anxiety in the general population and in daily clinical practice focus on age-related differences in the presentation of anxiety symptoms, a lack of help-seeking behavior in the present cohort of older adults, and age-related diagnostic problems met by professionals in general health care and in psychiatric settings. Older individuals themselves are not much inclined to seek mental health services for psychological problems (Waxman, Carner & Klein, 1984), but seem to remain in primary care settings (Klapow et al., 2002).

In the current study we want to focus on another problem that might contribute to the apparent lack of recognition of anxiety symptoms in older adults. In comparing anxiety in older versus younger adults, the assumption has typically been that the nature of anxiety and anxiety disorders is similar across different age groups. The validity of this assumption is unknown. Anxiety is the response that occurs when threat is perceived and it may differ between age groups on two crucial dimensions. First, the stimuli (CS) that elicit anxiety may differ. Older adults may tend to be anxious of different stimuli than younger adults. For example, specific stimuli might trigger fear in older adults, such as a hospital, a graveyard, or situations in which one might fall (darkness, a wet floor, steps and staircases). Secondly, the nature of feared misfortunes (UCS) may differ between age groups. This is the case when the same stimulus, for example the street, elicits anxiety in both younger and older adults, but

for very different reasons. A younger adult might avoid the street because of the fear to get a panic attack and faint; an older adult might avoid it because of the fear to fall and break a hip or the fear of being robbed.

Up to now little is known about the nature and experience of anxiety in the elderly, even though many authors claim that the phenomenology of anxiety may be different in older adults (e.g. Beck & Stanley, 1997; Fuentes et al., 2000). Research on the phenomenology of anxiety in older adults is still in its infancy and is limited to clinical impressions and a few recent studies.

As for the clinical impressions, authors mention several fears that seem to be typical for older adults, mostly in the sense of feared catastrophes. Fear of falling (Spano et al., 1992), fear of suffering from forgetfulness or dementia (Ponds et al., 1995), of becoming a victim of criminal assault (Clarke et al., 1982), fear of physical decline (illness, pain, going to a hospital), fear of losing autonomy, fear to lose one's partner and fear of being alone (Godderis et al., 1992) are examples of supposed geriatric anxieties. Clinical impressions suggest that fears in older adults concentrate around themes of loss, illness and disability, death and dying, and social changes.

There are only a few published experimental studies on qualitative differences in anxiety between younger and older adults. Liddell and others (Liddell, Locker & Burman, 1991) found that older adults (aged 50 years and over) mentioned more fear for the death of a beloved person, illness or injury of a relative, car-accidents, fights, and sudden premature death, making a fool of oneself and the fear to suffocate, than did younger adults, as measured by the Fear Survey Schedule (FSS-II; Wolpe & Lang, 1964). A recent epidemiological study (Gretarsdottir et al., 2004) on social anxiety showed that older adults (60-94 years) reported higher levels of anxiety in two situations: talking about business, and writing or typing in front of others. When analyses were repeated for a subgroup of the sample who scored high on social anxiety, older adults appeared to be significantly more anxious in five social situations: when speaking in a small informal meeting, when talking about business, when having to interact for longer than a few minutes with others, when writing or typing in front of others, and when attempting to avoid social situations where there

are others. Hunt (Hunt, Wisocki & Yanko, 2003) compared older adults (age 65-86) with younger adults on contents of worry and found that older adults expressed more worries about health, family concerns, and world issues than their younger counterparts.

Psychometric instruments to measure anxiety are largely based on mixed-age populations (18-65 years), which might not be suitable for measuring anxiety in older adults, since specific age-related fears may not be reflected in these instruments. Currently, two questionnaires have been designed to measure age-related worries and fears in late life. The Worry Scale (Wisocki, 1988) measures worry about finances, health and social conditions. However, in the study that validated this questionnaire only a small group of older adults participated that was relatively worry-free. Furthermore, a control group of younger adults was not included to ensure that items were truly age-specific. The second scale is the Anxiety about Aging Scale (Lasher & Faulkender, 1993). The 20 items measure fear of old people, psychological concerns, anxiety about physical appearance and fear of loss. Participants in the study were of all ages, but no significant age difference was found.

The purpose of the current study is to provide information about the nature of anxiety in older adults as compared to young and middle aged adults in the general population. More specifically, to get a better understanding of the fears of older individuals our question is twofold: do older and younger adults differ with respect to stimuli and situations that elicit fear, and is there a difference between age-groups with regard to the cognitive contents of anxiety in a particular situation? For this purpose, we have developed a new questionnaire, the Senior Anxiety Scale (SAS), to measure age-related worries in older adults. This scale was used along with other established measures of anxiety and worry. The current study also aimed to establish whether the SAS is a valid questionnaire for measuring the cognitive contents of worry in late life.

Methods

Participants and procedures

The study consisted of a mail-survey among the normal population aged 18 years and over in the Netherlands. Participants were involved from two different parts of the Netherlands, the Western urban part in and around the nation's capital Amsterdam with a very mixed population (region I), and the southern part of the country, the province of Limburg, a more rural and foremost Roman Catholic region (region II). When combined, these regions are considered to be representative of the Dutch population.

Participants from both regions were randomly drawn from the telephone book. The number of participants that was selected was proportionate to the number of inhabitants of the particular town. Every tenth address in the telephone book was called (3021 calls), 1359 people (45%) could not be included because they were not at home, they were not Dutch-speaking, or the number did not belong to a private person. Of the 1662 answered phone calls (55%), 615 subjects (37%) agreed to fill in questionnaires and 473 (70%) returned the questionnaire. The students who made these phone-calls used a standard text to invite the subject to participate in a study on anxiety.

All participants received a set of questionnaires and a return post-paid envelop. Their cooperation was awarded with a chance to win one of ten gift certificates of 25 Euro. When participants had not returned the questionnaire set within two weeks, they received a letter to remind them, in which they were kindly requested to complete the questionnaires.

At the onset of the study, everyone over 18 was requested to cooperate. At a later stage, persons were requested to cooperate depending on their age in order to keep the three age groups equal in size. Especially older male respondents were hard to find. For that reason, an additional set of 80 questionnaires was sent to members of the "Catholic Community for Older adults" (CCOA), a social club for retired older adults. 40 completed questionnaires were received (response rate 50%).

In total, 513 subjects participated in this study, 249 in the urbanized region and 264 subjects in the rural region of the Netherlands. Participants were divided in three age groups: young adults (18-44 years), middle-aged adults (45-64 years) and older adults (>65).

Measures

The Fear Survey Schedule (FSS; Wolpe et al., 1964; Arrindell, 1980) was chosen to measure fear-eliciting stimuli. The questionnaire contains 76 stimuli, grouped in seven subscales with a 5-point Likert-type scale (score 1-5): fear of noises (FSS-g); blood, death and somatic injury (FSS-b); agoraphobia (FSS-a); social phobia (FSS-s); fear of nature-phenomena (FSS-n); fear of harmless animals (FSS-an); and anxious ideations about sex and violence (FSS-sa). The Worry Domains Questionnaire (WDQ; Tallis, Eysenck & Mathews, 1992) can be considered as a measure of cognitive content of anxiety. The Dutch version, the Worry Domains Questionnaire-Revised (WDQ-R; van Rijsoort, Emmelkamp & Vervaeke, 1999) contains 30 questions with a 5-point Likert-type scale (score 1-5) on worries about five specific domains: relations (WDQrel), lack of self-confidence (WDQver), future (WDQfut), work (WDQinc), finances (WDQfin) and an additional 'health worry' domain (WDQhea). Because no scale on specific age-related anxiety and worry in older adults was available, a new scale was constructed on the basis of face- and expert validity. This scale was named the 'Senior Anxiety Scale' (SAS), but respondents were provided the questionnaire under the neutral name 'Anxiety Scale' to avoid possible bias. The SAS contains a selection from items from the Worry Scale (Wisocki, Handen & Morse, 1986) transformed as 'anxiety' questions, items from the Anxiety about Aging Scale (Lasher et al., 1993), items that were derived from our own clinical practice with older patients and items based on the available literature on late-life anxiety. It is composed of 77 questions on a 5-point Likert-scale (score 1-5); the last five items are only to be answered if the subject has children and/or a (living) partner. The Eysenck Personality Questionnaire-revised, N-subscale (EPQ-R (Eysenck & Eysenck, 1968; Eysenck, Eysenck & Barret, 1985)) with 12 yes/no items was included in the set to

control for an overall tendency to be anxious as a possible confound. Demographic information was gathered through the administration of a biographical questionnaire, a simple structured list of questions on age, gender, country of birth of the subject and his/her parents, marital status, living situation, level of education and religion. Educational level was measured by a Dutch scoring system that consists of a 7-point scale ranging from primary education (level 1) to university education (level 7).

Sample characteristics

Participants ($N=513$) were almost equally distributed over the three age groups (see table 1). Age ranged from 19 to 92 years. Female subjects were overrepresented, but this overrepresentation was similar in all age groups. Marital status differed between age groups, with a higher proportion of older adults living alone, compared to the young and middle-aged group ($\chi^2=54.9$, $df=2$, $p<.001$). We found an age related decline in level of education ($F=23.9$, $df=2,508$, $p<.001$). The three age groups did not differ with respect to religion, or in the mean score on neuroticism as measured with the EPQ-R.

Participants from both regions were compared with respect to demographic variables. Region samples did not differ with respect to age. Participants from both regions did differ with respect to sex (in region II women were overrepresented ($\chi^2=7.36$, $df=1$, $p<.01$); education (educational levels 3, 4 and 5 (representing medium education) were more prevalent in region II ($\chi^2=20.70$, $df=6$, $p<.01$) whereas in region I there were more subjects with a university level of education); religious background ($\chi^2=227.44$, $df=2$, $p<.001$; Roman Catholics were overrepresented in region II whereas in region I subjects often stated not to have any religion) and marital status (in region II significantly more subjects were living together with a partner ($\chi^2=8.86$, $df=1$, $p<.01$). Sex, level of education, religion and marital status will be included as co-variates in the analyses.

Table 1. The distribution of descriptive variables across the three age groups.

N=513	I. Young (19-44 years) N= 170	II. Middle-aged (45-64 years) N=174	III. Old (>65 years) N=169
Mean age (SD)	34.7 (5.8)	53.9 (5.7)	73.4 (6.1)
Female	103	101	93
Male	67	73	76
Living alone	40	30	89
Living together	128	140	80
<i>Level of education</i>			
Elementary	3	7	21
Elementary + few yrs ¹	0	11	20
Lower vocational	18	42	23
General intermediate	32	39	38
Intermediate vocational	34	19	19
General secondary	7	7	13
Higher vocational/university	76	47	35
Mean level (SD)	5.5 (1.6)	4.5 (1.8)	4.1 (2.0)
<i>Region</i>			
Amsterdam	90	79	80
Limburg	80	95	89
<i>Religion</i>			
Roman Catholic	90	101	93
other	27	32	37
none	53	41	39
Mean neuroticism score	1.46	1.47	1.47

Characteristics of the subsample from the Catholic Community for older adults (CCOA)

The participants from the 'Catholic Community for older adults' were included because of the lack of older participants, especially male older participants.

¹ Elementary education plus a few years of general intermediate or secondary education (not completed)

Compared to the older adults selected by the phone book ($N=129$) in age group III, the CCOA-subjects ($N=40$) appeared to be significantly younger with a mean age of 71 ($SD=4.3$) vs. 74 years ($SD=6.4$), $F=9.111$, $p<.005$. In the CCOA-sample women were overrepresented ($\chi^2=.029$, $df=1$, $p=.05$), whereas in the older sample recruited by telephone the distribution of the sexes was nearly equal. The CCOA participants had a higher educational level; level 5, 6 and 7 were overrepresented ($\chi^2=.049$, $df=6$, $p=.05$).

Statistical Analyses

Data were analyzed using SPSS-11. Age groups were compared on demographic variables (gender, marital status, level of education, religion) and neuroticism using ANOVAs. For all questionnaires, the mean total item score and the mean subscale item scores were calculated. A Principal Components Analysis with obimin rotation was conducted on the newly constructed Senior Anxiety Scale. For all scales and subscales Cronbach's alpha was computed to determine their level of internal consistency. Missing data were imputed by means of a "Missing Value Analysis" in SPSS so that all questionnaires could be included in the analyses. Univariate Analyses of Variance (ANOVAs) were conducted to explore the differences in mean raw total and subscale scores on the three questionnaires (FSS, WDQ-R and SAS) between the three age groups. ANCOVAs were conducted using region, sex, level of education, marital status and religion as covariates because the two regions, the three age groups and the CCOA group differed with respect to these variables. When the corrected F-test proved significant, post-hoc t-tests were done to determine specific group differences. Bonferroni correction was applied on all analyses because of multiple testing, which means for the FSS that the p-value was multiplied by seven (the number of subscales), for the WDQ by 5, and for the SAS by 4. The significance of mean differences was set at $p<.05$ after correction.

Results

Factor structure of the Senior Anxiety Scale (SAS)

The analysis of the SAS indicated that a four-factor solution was the best fit to the data. From the 77 items only 72 items were involved in the analyses, because the last five items were exclusively applicable to participants with a living partner and children. Items were selected if their factor loading was at least .50 and the loading on any of the other factors was smaller than .30; only three out of 72 items loaded less than .40 on one of the factors. These three items were excluded from further analyses. The correlation between the three factors was between .4 and .5; factor 4 correlated lowest with the other factors.

The total explained variance of the four-factor solution was 54.7 %. Factor 1 (33 items, Cronbach's $\alpha=.97$) explained 43 % and refers to fear of decline of physical and mental health and loss of independence. Examples of items loading on this factor include: 'I'm afraid of falling and breaking something', 'I'm afraid to forget important things', 'I'm afraid I won't be able to drive my car anymore'. Factor 2 (7 items, Cronbach's $\alpha=.91$) refers to the fear of financial problems and explained 1.5% of the total variance. Examples of items for the second factor include: 'I'm afraid I will hardly be able to make ends meet when I am old' and 'I'm afraid I won't be able to pay my insurance-premium'. Factor 3 (explained variance 3%, 20 items, Cronbach's $\alpha=.93$) reflects the fear of social isolation or social disapproval. Examples of items include: 'I'm afraid I will be alone', 'I'm afraid that people will find me unattractive'. Factor 4 (explained variance=3%, 9 items, Cronbach's $\alpha=.92$) is associated with the fear of life-threatening situations (deadly illness, dying and crime). Examples of items include: 'I'm afraid to die', 'I'm afraid to get a heart attack', 'I'm afraid I will be robbed on the street'.

In summary, this questionnaire appears to be a strong measurement instrument with a high internal consistency, rendering it appropriate to compare different groups.

Comparison between age groups on the FSS, WDQ and SAS

Table 2 presents results from the ANCOVAs and post-hoc t-tests. The total score and all mean subscale scores of the FSS, except the FSS-B (the fear of blood, injections, and dead people), differed significantly between the three age groups. On the total FSS-scale (FSS-tot) the older ($t(337)=3.64, p=.001$) and middle-aged subjects ($t(336)=3.95, p<.001$) scored significantly higher than the youngest group, but there were no significant differences between older adults and the middle-aged group. Similar results were found for the FSS-G (fear of noises; Cronbach's $\alpha=.90$; $t(337)=3.74, p<.001$ and $t(336)=3.37, p=.009$ resp.), the FFS-A subscale (agoraphobic fears (Cronbach's $\alpha=.92$; $t(337)=3.74, p<.001$ and $t(336)=4.04, p<.001$ respectively), the FSS-N (the fear of nature-phenomena, Cronbach's $\alpha=.82$; $t(337)=3.51, p<.001$ and $t(336)=3.52, p<.001$ resp.), and the subscale FSS-AN (fear for harmless animals ; Cronbach's $\alpha=.80$; $t(337)=3.58, p=.001$ and $t(336)=2.63, p=.028$, resp.). On the subscale FSS-S (the fear of social situations; Cronbach's $\alpha=.79$) the scores of the young adult group were significantly lower than the middle-aged group ($t(336)=2.77, p=.016$), but no significant differences were found between older adults and middle-aged subjects or between older adults and the young adult group. The only subscale that differentiated between both older adults and the middle-aged group and between the middle-aged and young adult group was the FSS-SA measuring fear of sex and aggression, with older adults scoring higher than middle-aged subjects ($t(337)=2.51, p=.039$ and middle-aged subjects scoring higher than young adults ($t(336)=4.37, p<.001$).

The three age groups did not differ on the total score of the WDQ (Cronbach's alphas of the subscales were between .70 and .90) or on any of the WDQ subscales except for the subscale WDQ-fin (worry about financial matters). The youngest subjects and the middle-aged scored significantly higher ($t(337)=2.43, p=.044$ and $t(337)=2.46, p=.043$ resp.) on worry about finances than the older subjects.

The total score on the Senior Anxiety Scale (SAS-tot) increased significantly with age (group young<middle-aged, $t(336)=3.06, p=.007$; group middle aged<old, $t(337)=2.51, p=.037$). When analyzing the different factors, Factor 1, the fear of physical and

mental decline, was found to increase significantly with age (group young<middle-aged, $t(336)=4.0$, $p<.001$; group young<old $t(337)=7.88$, $p<.001$; group middle-aged<old, $t(337)=4.20$, $p<.001$). Factor 2 (the fear of financial problems) and factor 3 (the fear of social isolation and disapproval), both showed no significant differences between the three groups. On factor 4, representing the fear of life threatening situations (serious illness, death and criminality), older adults scored significantly higher than the youngest group ($t(337)=3.67$, $p=.001$).

Table 2. ANCOVAs and post hoc t-tests comparing the three age groups.

N=513 (19-92 years)	I Young (19-44 yrs) M.I.S. ² (SD)	II.Middle (45-64 yrs) M.I.S. (SD)	III. Old (>65 yrs) M.I.S. (SD)	Analysis of variance (F, p)	Post-hoc t- test Bonferroni
FSS-G (noises)	1.32 (.60)	1.56 (.59)	1.53 (.60)	F(2,496)=7.86,p<.001** ³	I < II and III
FSS-B (blood, injections)	1.89 (.70)	2.06 (.69)	1.89 (.71)	F(2,496)=3.13,p=.045	
FSS-A (agoraphobic stimuli)	1.44 (.53)	1.67 (.52)	1.67 (.55)	F(2,496)=10.02,p<.001**	I < II and III
FSS-S (social stimuli)	1.80 (.71)	2.02 (.70)	1.99 (.73)	F(92,496)=4.40,p=.013**	I < II
FSS-N (natural phenomena)	1.61 (.78)	1.91 (.76)	1.92 (.79)	F(2,496)=8.25,p<.001**	I < II and III
FSS-AN (harmless animals)	1.55 (.69)	1.75 (.67)	1.83 (.69)	F(2,496)=6.91,p<.001**	I < II and III
FSS-SA (sex and aggression)	1.64 (.67)	1.96 (.66)	2.14 (.69)	F(2,496)=22.27,p<.001**	I < II < III
FSS-tot (total)	1.66 (.54)	1.89 (.53)	1.88 (.55)	F(2,496)=9.61,p<.001**	I < II and III
WDQ-rel (relations)	1.52 (.66)	1.53 (.65)	1.42 (.68)	F(2,496)=1.22, p=.296	
WDQ-ver (lack of confidence)	1.74 (.86)	1.74 (.84)	1.67 (.89)	F(2,496)=.322, p=.725	
WDQ-fut (aimless future)	1.54 (.78)	1.70 (.77)	1.64 (.79)	F(2,496)=1.82, p=.163	
WDQ-inc (work incompetence)	1.66(1.04)	1.69(1.02)	1.61(1.07)	F(2,496)=.228, p=.796	
WDQ-fin (finances)	1.59 (.73)	1.58 (.71)	1.38 (.74)	F(2,496)=3.899,p=.021**	I and II > III
WDQ-lic (Physical)	1.80 (.95)	1.95 (.93)	1.99 (.96)	F(2,496)=1.834,p=.161	
WDQ-tot (total)	1.64 (.65)	1.70 (.64)	1.62 (.66)	F(2,496)=.68,p=.508	
SAS: physical and mental decline,	1.38 (.75)	1.71 (.74)	2.06 (.77)	F(2,496)=31.03,p<.001**	I < II < III
SAS: financial problems	1.33 (.62)	1.38 (.61)	1.21 (.63)	F(2,496)=2.74, p=.065	
SAS: social isolation and disapproval	1.35 (.58)	1.44 (.57)	1.43 (.59)	F(2,496)=1.16, p=.313	
SAS: life threatening situations	1.77 (.89)	1.96 (.88)	2.15 (.91)	F(2,496)=6.84, p=.001**	I < III
SAS-tot (total)	1.43 (.64)	1.64 (.62)	1.81 (.65)	F(2,496)=14.33,p<.001**	I < II < III

² M.I.S. = Mean Item Score³ **significant after adjustment for multiple comparisons Bonferroni.

Discussion

The current study was carried out to examine differences in the nature of anxiety between various age groups. This study was the first to make a distinction between fear-eliciting stimuli (measured by the FSS), and feared catastrophes in a particular situation (measured by the WDQ-R and SAS). The Senior Anxiety Scale (SAS) was uniquely designed to measure feared catastrophes in older adults.

Looking for differences in fear-eliciting stimuli of the FSS, there was a significant difference between the three age groups on the total score and on all subscales, except for the FSS-B, the fear of blood, injections and dead people. Older adults and middle-aged subjects were clearly more anxious of stimuli in general and they showed more fear of noises, agoraphobic situations, nature phenomena and harmless animals than the youngest group of subjects. Social situations elicited more fear in the middle-aged group. It is conceivable that this finding arises from the fact that middle-aged subjects meet more life circumstances where social anxiety is easily provoked while older adults come across such situations less often. These results are in concordance with results from a previous study on the phenomenology of social anxiety in older adults, in which social anxiety appeared to be less frequent in older individuals (Gretarsdottir et al., 2004). The fear of sexual and aggressive scenes increased significantly with age (as was expected; at least for aggression). In summary, older adults are more anxious of a variety of stimuli than younger adults, but most differences appear to develop before the age of 65. The FSS can therefore be seen as a sensitive instrument to detect fear-eliciting stimuli in older adults, but it shows no specificity for an older population.

With regard to feared catastrophes or cognitive contents it was remarkable that the WDQ-R did not differentiate between the three age groups on the total questionnaire nor on the subscales, except for the worry about financial matters. The young adults and the middle-aged subjects were more anxious about their financial situation than the older adult group. This may be a result of the fact that pension arrangements in the Netherlands tend to be quite beneficial. As for the other subscales, subjects of all ages seemed to worry about the same topics to the same extent.

On the newly constructed questionnaire designed to measure age-related feared catastrophes in older adults, the SAS, we found that the total score was highest in older adults, which provides support for the validity of this questionnaire as a specific measure for late-life anxiety. Especially the fear of physical and mental decline increased significantly with age. In contrast to the WDQ-finance subscale, the fear of financial problems as measured by the SAS, showed no significant difference between the three groups. In contrast to our expectations based on our clinical impressions, we found no differences between the three age groups with regard to the fear of social isolation and disapproval. On factor 4 of the SAS, the fear of life-threatening situations (serious illness, death and criminality) the older adult group scored significantly higher than the young adult group. This is in line with the hypothesis that older adults tend to be afraid of becoming a victim of criminal assault (Clarke et al., 1982) and the common sense notion that older adults tend to be afraid of death and dying. In clinical practice, older adults usually mention that they are more afraid of the way they might die (with pain and anguish), than of death itself.

Our findings confirm the clinical impressions and earlier studies on anxiety in older adults, which suggest that fears in this age group concentrate around themes of experiences of loss (especially loss of autonomy), physical and mental illness, death and dying, criminal assault and aggression. Specific 'geriatric' fears are important to take into consideration, because they can lead to activity limitation and avoidance behavior comparable to 'normal' anxiety disorders. For example, the fear of falling can lead to avoidance behavior that resembles agoraphobia. Similarly, the fear to forget things, the so called 'dementia-phobia' (Ponds et al., 1995) can lead to a pattern of anxiety and avoidance behavior that resembles social phobia. The acknowledgement of these fears has already led to specific therapeutic interventions, in the form of a course for older adults who suffer from the fear of falling (Haastregt & Zijlstra, 2002) and a short intervention for older adults who are afraid they might develop dementia in spite of good results on psychiatric examination and neuropsychological tests (Ponds et al., 1995).

The fact that the FSS did not differentiate between middle aged and older adults, makes one wonder in what stage in life the apparent shift in fear-eliciting stimuli occurs. The cut-off of 65 years for the older group is based on the approximate age of retirement. In the literature nowadays many different cut-offs are used indicating older adults, including individuals as young as 55. The switch in fear-eliciting stimuli probably takes place at an earlier age than 65.

In summary, our results suggest that it is important to ask age-specific questions in order to detect anxiety in older adults. The SAS appears to be a valid instrument with high internal consistency suitable for this purpose. The differentiation between feared stimuli and feared catastrophes or cognitive content has proven meaningful. Our results indicate that the largest difference between younger and older adults lies in the cognitive contents of anxiety. However, we cannot conclude on the basis of our study that it is not possible to detect specific fear-eliciting stimuli for older adults. The FSS may not include items that are specifically important for anxiety in late life. It would be interesting to develop a scale with fear-eliciting stimuli that might be more relevant to situation of older persons, in the same way that we constructed the SAS to measure age-related feared catastrophes. The authors of the previously mentioned study on the phenomenology of social anxiety (Gretarsdottir et al., 2004) also suggest that current measures of social anxiety probably do not include some of the most anxiety-provoking situations for older adults.

One of the limitations of this study concerns the fact that stimuli and feared catastrophes are not connected. It would be interesting to find out whether certain stimuli evoke specific age-related feared catastrophes. Also it could be worthwhile to conduct open-ended personal interviews on feared stimuli and cognitive contents of anxiety with older and younger adults, as a valuable completion to self-report measures.

Meanwhile it is stressed that while the present data give an indication of age-related differences in anxiety in the population at large, the study does not provide data on age-related differences in anxiety in clinical groups. Though it is an open question if and to what degree the present results can be generalized to clinical populations, the

factor structure of the FSS is comparable in clinical and non clinical groups (Arrindell et al., 1990; Arrindell & van der Ende, 1986) and it seems plausible to expect a comparable pattern in patients with clinical anxiety problems. However, this is an empirical issue that awaits investigation.

Our findings carry important implications for the diagnosis and treatment of late-life anxiety. Older adults with anxiety symptoms show a high and inappropriate use of health care services and medication and their quality of life is greatly affected (de Beurs et al., 1999). Early detection of anxiety might increase appropriate referral and help prevent a chronic course of late-life anxiety. To screen carefully for anxiety in the older adults, taking into account scientific knowledge of age-related fear-eliciting stimuli and feared catastrophes might not only improve diagnosis, it could also give relevant information for a tailor-made psychological intervention.

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Chapter 3



The outcome of anxiety disorders in older people at six-year follow-up: results from the Longitudinal Aging Study Amsterdam.

Abstract

Objective: To examine long-term outcome of late-life anxiety disorders and utilization of mental health care services. **Method:** A cohort of subjects (aged ≥ 55 years) with an anxiety disorder ($n=112$) was identified in the Longitudinal Aging Study Amsterdam ($N=3107$). At six-year follow-up, the rate of persistence and prognostic factors for persistence of anxiety were established. **Results:** Six years after baseline 23% of our sample met the criteria for an anxiety disorder. Another 47% suffered from subclinical anxiety symptoms. Persistence of anxiety was associated with a high score on neuroticism at baseline. Use of benzodiazepines was high (43%), while use of mental health care facilities (14%) and anti-depressants (7%) remained low in those with persistent anxiety. **Conclusion:** Results indicate that those high in neuroticism are at greater risk for persistence of anxiety. Efforts to enhance appropriate referral of anxious older adults do not seem to have had the desired effect.

This chapter has been published as:

Schuurmans, J., Comijs, H. C., Beekman, A. T. F., de Beurs, E., Deeg, D. J. H., Emmelkamp, P. M. G. et al. (2005). The outcome of anxiety disorders in older people at six-year follow-up: results from the Longitudinal Aging Study Amsterdam. *Acta Psychiatr.Scand.*, 111, 420-428.

Although the number of studies dealing with the psychological well-being of older people has increased considerably, most of these studies have focused on depression. This reflects a commonly held belief in geriatric psychiatry that mood disorders are more prevalent in older adults than anxiety disorders. However, recent epidemiological studies have shown that anxiety disorders are in fact more common in older adults than major depression and dysthymia (Regier et al., 1988; Beekman et al., 2001). The prevalence of anxiety disorders in older adults is estimated at 10% (Beekman et al., 1998), which is comparable to the prevalence of anxiety disorders in younger age groups in the Netherlands (Bijl et al., 1998). Furthermore, recent studies have shown that anxiety greatly affects the quality of life in older persons (Wetherell et al., 2004) and that it is also associated with an increased use of (non-mental) health care services, even when controlling for physical health status (de Beurs et al., 1999).

Studies focusing on younger populations have demonstrated that anxiety disorders show a chronic but variable course with intermittent periods of waxing and waning of symptoms when left untreated. Spontaneous remission rates in these studies range from 12 to 25% (Angst et al., 1991). No data are available on the rates for remission and persistence of anxiety disorders in older adults.

The present study is part of an ongoing longitudinal community based study on autonomy and well-being in older adults, aged 55 to 85 years in the Netherlands (the Longitudinal Aging Study Amsterdam (Deeg, Knipscheer & van Tilburg, 1993; LASA). In a previous 3-year follow-up study by our research group on risk factors for persistence of anxiety symptoms in older adults, female sex and neuroticism were found to increase the likelihood of persistence of anxiety. Other variables, such as health status, socio-economic status, social resources and life events were found to be unrelated to the outcome of anxiety symptoms in older people (de Beurs, Beekman, Deeg, van Dyck & van Tilburg, 2000). However, at 3-year follow-up of the LASA study, measurements did not include psychiatric diagnosis. Instead the score on a questionnaire for anxiety (the HADS-A; Zigmond & Snaith, 1983) was used to divide the sample into a non-anxious group and a group with anxiety symptoms.

In spite of the increased use of health care services, anxious older people are rarely referred to mental health care (de Beurs et al., 1999). For the most part, anxiety disorders in older people are left untreated (and probably unrecognized). The only common form of treatment appears to be the prescription of benzodiazepines (de Beurs et al., 1999), even though most clinicians and researchers agree that long-term use of benzodiazepines is best avoided, especially in older adults (Flint, 1997; Salzman, 1990). Regardless of the possible risks of long-term use of benzodiazepines, such as memory impairment and an increased risk of accidents and falls (Lader, 1999; Petrovic, Mariman, Warie, Afschrift & Pevernagie, 2003) the high risk for development of tolerance and dependence are important disadvantages (Kan, Breteler & Zitman, 1997). Modern serotonin-based antidepressants, that have been proven effective in mixed-age populations (van Balkom, 2000), do not carry the same risk for development of dependence (van Broekhoven, Kan & Zitman, 2002). Nevertheless, they are rarely prescribed to older adults. In recent years several efforts have been made to lower long-term use of benzodiazepines in older adults and to enhance recognition and appropriate referral of anxious older adults, but we have no data on whether these efforts have paid off.

In LASA, a subgroup (n=112) of older persons with anxiety disorders has been identified and reports have been made on comorbidity patterns, utilization of health care services, physical functioning and quality of life. The present study reports on the outcome of anxiety and the utilization of mental health care services and anxiolytic medication by this group, after a follow up period of six years.

Aims of the study

Research questions were as follows: What is the long-term outcome of anxiety disorders in older persons? What factors are predictive for persistence of anxiety? Is a persistent outcome of anxiety disorders related to an adequate use of mental health care services and has the use of benzodiazepines decreased?

Material and methods

Sample

Data were derived from the Longitudinal Aging Study Amsterdam (LASA). A random sample, stratified on age and sex, was drawn from population registers in 11 municipalities in three regions of the Netherlands. Ten months prior to LASA, respondents had participated in the NESTOR-study on Living Arrangements and Social Networks for older adults, which had a response rate of 62.3% ($n=3805$). All participants of the NESTOR-study were approached for the first LASA cycle. 3107 (81.7%) subjects were enrolled in the baseline LASA interview, which took place between September 1992 and September 1993 (T1). Attrition was related to age, but not to sex. Subjects with anxiety disorders were identified using a two-stage screening design. The Centre for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977) was used as screening instrument for depression and anxiety. The CES-D has been found to be a good screener for anxiety (Breslau, 1985). All subjects scoring ≥ 16 ($n=386$) and a similarly sized random sample of those scoring < 16 ($n=380$) were selected for the second stage, which involved a diagnostic interview, held 2 to 8 weeks after the first LASA assessment. Response was 86%, leaving a sample of 659 subjects, 332 screen positives and 327 screen negatives, to be interviewed. Anxiety disorders were defined according to DSM-III criteria and assessed by means of the Diagnostic Interview Schedule (DIS; Robins, Helzer, Croughan & Ratcliff, 1981). A total of 112 subjects met the criteria for an anxiety disorder in the last 6 months prior to the interview (Beekman et al., 1998). Those with comorbid depression (26%; $n=29$) were not excluded. All measurements in this report are based on this sample.

Follow-up took place in 1998-1999 (T2), six years after the baseline measurement. During follow-up 50 of the 112 subjects with a diagnosed anxiety disorder at T1 were lost, leaving a sample of 62 subjects who completed the second diagnostic interview (55% of the original sample). Attrition was largely due to death ($n=32$, 29% of the original sample and 64% of the total attrition rate). 7% ($n=8$) refused to participate further, another 7% ($n=8$) were ineligible due to illness or cognitive impairment and

2% (n=2) could not be contacted for follow up due to migration. Variables associated to loss to follow up are described in the results section of this article.

Measures

Assessment of outcome of anxiety

Anxiety disorders were defined according to DSM-III criteria and assessed by means of the Diagnostic Interview Schedule (DIS; Robins et al., 1981). In this study four types of anxiety disorders were distinguished: phobic disorders, panic disorder, generalized anxiety disorder and obsessive-compulsive disorder. Subsyndromal anxiety was defined as the presence of clinically relevant anxiety symptoms without meeting the diagnostic criteria for an anxiety disorder according to the DIS. In accordance with previous research by our group (de Beurs et al., 1999), the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A; Zigmond et al., 1983) was used to discriminate those with subsyndromal anxiety from those with no relevant anxiety symptoms. A score halfway between the mean score for the entire sample (N=3056) and the mean score of subjects with an anxiety disorder was chosen as a cut-off score, since no threshold score for the Dutch version of the HADS-A was available to delineate clinical anxiety. The cut-off point was a score between 3 and 4 (de Beurs et al., 1999). Sensitivity of this cut-off was 58% and specificity 80%, for 6-month prevalence of any DSM-III anxiety disorder (de Beurs et al., 2000). For the outcome of anxiety disorders six years after baseline three possibilities were distinguished: i) Persistent anxiety: respondents who met criteria for an anxiety disorder at both measurements; ii) Partial remission of anxiety: respondents who did not fulfill diagnostic criteria for an anxiety disorder at T2 but who did suffer from subsyndromal anxiety; iii) Full remission: respondents who did not meet criteria for either an anxiety disorder or subsyndromal anxiety at T2.

Prognostic factors

Selected prognostic factors for persistence of anxiety were divided into six groups: demographic variables, variables regarding physical health and functioning, illness severity, personality characteristics, social support, treatment and life changes.

Demographic variables included age, sex, level of education, socio-economic status and marital status. To establish socio-economic status a weighted score composed of the level of education, occupation and income (range 0-100) was used (van Tilburg, Dijkstra, Liefbroer & Broese van Groenou, 1995). The presence of chronic diseases was assessed by asking the respondents explicitly whether they suffered or had suffered from any of the following chronic diseases or disease events: cardiac disease (including myocardial infarction), peripheral arthrosclerosis, stroke, diabetes mellitus, chronic obstructive pulmonary disease (COPD: asthma, chronic bronchitis or pulmonary emphysema), arthritis (rheumatoid arthritis or osteoarthritis) and cancer. In a previous study, the validity of this instrument was supported by the records of respondents' general practitioners (Kriegsman, Penninx, van Eijk, Boeke & Deeg, 1996). In the present study, we focused on the number of chronic diseases as a possible predictor for outcome of anxiety. Other variables regarding physical health included in this study were a subjective health rating (CBS, 1989) and functional limitations assessed with an adaptation of the Organization of Economic Collaboration and Development Questionnaire (OECD; van Sonsbeek, 2004). Cognitive functioning was measured with the Mini-Mental State examination (Folstein, Folstein & McHugh, 1975). The scale consists of 23 items, which are used to measure global cognitive performance. Scores range from 0-30, with a cut-off score of ≤ 23 as an indicator for cognitive impairment. Alcohol use was assessed during an interview with a questionnaire developed by the Dutch Central Bureau of Statistics. If respondents drank alcohol, they were asked how many days a week they drank alcoholic beverages and how many glasses they would usually drink each time. On the basis of these data, alcohol use was categorized as light (average consumption one unit per day), moderate (average consumption 2-3 units per day), excessive

(average consumption 4-5 units per day) or very excessive (average consumption 6 or more units per day; Garretsen, 1983).

Personality characteristics included neuroticism, social inadequacy (dislike and avoidance of social interaction), mastery and self-efficacy. Neuroticism and Social Inadequacy were measured with the abbreviated subscales of the Dutch Personality Inventory (Luteijn, Starren & van Dijk, 1985). Mastery was measured with the abbreviated 5-item 'mastery' scale (Pearlin & Schooler, 1978) and self-efficacy was measured with the 12-item version of the General Self-Efficacy Scale (Sherer et al., 1982; Bosscher & Smit, 1998). Social support was defined as the reception of both instrumental and emotional support and was measured by a questionnaire which included detailed questions on both the number and the quality of contacts with members of the social network (van Tilburg, Dijkstra & Broese van Groenou, 1992).

In interviews three years and six years after baseline respondents were asked whether stressful life-events had occurred in the three year time interval prior to the interview. The following stressful events were assessed: Illness of one's partner, death of one's partner, illness of a relative, death of a relative, a major conflict with others, income loss, victimized by crime, and relocation. Other life stressors were derived from data at both the baseline and follow-up measurements: declined physical health (developing a new or additional chronic disease); an increase in functional limitations (≥ 1 points increase on the scale) and cognitive decline (> 5 points deterioration on the MMSE; (Schmand, Lindeboom, Dinkgreve, Hooijer & Jonker, 2004). To reduce the number of variables in analyses regarding life events, a composite score (labeled as 'level of distress') was computed by differentially weighing life-events and combining them in one score, representing the impact of the events. Weights for the various life-events were derived from Tennant and Andrews (Tennant & Andrews, 1976). All scales used in the study had been previously validated in the Netherlands or else their psychometric properties had been evaluated in LASA pilot studies (Deeg et al., 1993).

Mental health care service utilization and use of anxiolytic medication

Subjects were interviewed about recent visits to physicians, to community health care services, to paramedical services, to formal social support and hospital admissions. In order to reduce the number of variables in the analyses, a composite score labeled as 'mental health care' was computed, reflecting whether or not a respondent had recently visited a psychiatrist, a community mental health care service, a social psychiatric service or a social worker. Furthermore, subjects were interviewed about their use of medication, and the response was ascertained by inspecting the bottles of currently prescribed medication during the home visit. Data on anxiolytic medication were grouped into two categories: i) Use of benzodiazepines; ii) Use of antidepressants.

Statistical analysis

To check for selective attrition we compared the 62 participating subjects with the 50 drop-outs on all variables included at baseline with chi-square tests or t tests. Means, standard deviations and percentages for the distribution of all relevant variables across the three outcome groups (persistent anxiety, partial remission and full remission) were computed. To investigate the prognostic value of demographic and clinical variables measured at baseline for the outcome of anxiety, a series of logistic regression analysis were run. In the first series of analysis, respondents with persistent anxiety were compared with respondents who were in full remission. In the second series, respondents who suffered from subsyndromal anxiety (partial remission) were compared with respondents who were in full remission. The strength of the association between prognostic factors and outcome of anxiety at T2 was expressed in odds ratios (ORs). To control for the influence of sex, age and chronic disease a series of multiple logistic regression analyses were performed in which these potentially confounding variables were entered individually in the models.

Results

Characteristics of the sample

Loss to follow-up was associated with higher age, male sex, more chronic diseases, more functional limitations and a lower level of cognitive functioning at baseline. Loss to follow-up was not associated with a higher score on anxiety or depressive symptoms at baseline. Of the original sample of respondents with an anxiety disorder at baseline ($n=112$), 70% ($n=77$) had a generalized anxiety disorder at baseline, 32% ($n=36$) had a phobic disorder (this category included agoraphobia), 21% ($n=23$) had a panic disorder and 8% ($n=9$) had an obsessive-compulsive disorder. GAD and phobias have been found to be the most prevalent anxiety disorders among older adults (Beekman et al., 1998b; Flint, 1994a). Means, standard deviations and percentages for the distribution of all relevant variables measured at baseline across the three groups representing different outcomes of anxiety are presented in Table 1 (next page).

The outcome of anxiety

At follow up, 13% ($n=14$) had an anxiety disorder, 26% suffered from subsyndromal anxiety ($n=29$) and 17% ($n=19$) were in full remission of anxiety. Twenty-nine percent ($n=32$) were deceased during follow up and 16% ($n=18$) were lost to follow up due to other reasons.

Thus, of the sample used in the analyses ($n=62$), 23% had a persistent outcome of anxiety, 47% were in partial remission and 31% were in full remission of anxiety. Due to small sample size, anxiety disorders were not categorized into different subtypes.

Table 1. Distribution of predictor variables measured at baseline
over different types of outcome.

	Persistent anxiety (n=14)	Partial remission (n=29)	Full remission (n=19)	Total (n=62)
<i>A Demographic characteristics</i>				
Sex (% female)	85.7	82.8	63.2	77.4
Age (yrs; M (SD))	67.4 (8.6)	69.7 (8.6)	73.1 (8.7)	70.2(8.7)
Marital status (% married)	50.0	41.4	52.6	46.8
Socio-econ. status (M (SD))	24.9 (13.4)	24.7 (17.4)	36.8 (17.4)	28.5 (17.6)
<i>B Psychological symptoms</i>				
Anxiety score (M (SD))	11.2 (5.0)	7.7 (5.2)	8.3 (4.5)	8.6 (5.1)
Depressive sympt. (M(SD))	26.3 (9.5)	21.3 (11.3)	21.0 (10.8)	22.3 (10.8)
<i>C Personality characteristics</i>				
Mastery (M (SD))	13.7 (3.8)	14.1 (3.5)	15.8 (3.3)	14.5 (3.6)
Perceived self-efficacy (M(SD))	36.6 (5.9)	39.0 (5.8)	38.5 (5.0)	38.3 (5.6)
Neuroticism (M (SD))	18.6 (7.2)	11.7 (6.2)	10.3 (6.7)	12.7 (7.1)
Social Inadequacy (M (SD))	11.6 (6.1)	7.7 (5.5)	9.3 (5.9)	8.9 (5.8)
<i>D Social functioning</i>				
Emotional support (M (SD))	1.9 (.9)	1.6 (.8)	2.0 (.4)	1.8 (0.7)
Loneliness (M (SD))	3.5 (4.0)	4.4 (3.6)	4.6 (3.1)	4.3 (3.5)
<i>E Health status</i>				
Nr. chronic diseases (M(SD))	2.2 (1.3)	1.5 (1.1)	1.8 (1.6)	1.8 (1.3)
Self-perceived health (M (SD))	3.1 (1.0)	3.1 (1.1)	2.8 (.7)	3.1 (1.0)
Functional limitations (M(SD))	1.1 (1.0)	1.2 (1.1)	.9 (1.1)	1.1 (1.1)
Cognitive functioning (M(SD))	27.8 (1.4)	26.7 (2.6)	27.3 (2.3)	27.1 (2.3)
Alcohol use (%)				
No alcohol use	21.4	31.0	15.8	24.2
Light	57.1	55.2	57.9	56.5
Moderate	21.4	10.3	15.8	14.5
Excessive	0.0	3.4	10.5	4.8
<i>F Stressor variables</i>				
Level of distress (M(SD))	67.5 (42.7)	59.1 (44.6)	56.8 (35.0)	60.1 (40.8)
Incr. in chronic diseases (%)	21.4	55.2	50.0	45.9
Incr. in functional limitations(%)	42.9	25.0	42.1	34.4
Cognitive decline (%)	0.0	3.6	5.3	3.3

Prognostic factors for persistence or remission of anxiety

Table 2 presents bivariate odds ratios and 95% confidence intervals for all possible prognostic factors for the different types of outcome of anxiety (i.e. persistent anxiety, partial remission or full remission).

Table 2. Prognostic factors for outcome of anxiety measured at baseline (n=62)

	Persistence of anxiety n=14		Partial remission n=29	
	OR	95% CI	OR	95 % CI
<i>Demographic variables</i>				
Female sex	3.5	.60 – 20.41	2.80	.73 – 10.69
Age	.93	.85 – 1.01	.95	.89 – 1.02
Not/no longer married	.90	.23 – 3.58	1.57	.49 – 5.05
Socio-economic status	.95	.91 – 1.00	.96	.93 – .99
<i>Health status</i>				
Chronic diseases	1.23	.75 – 2.01	.86	.55 – 1.35
Perceived health	1.56	.66 – 3.70	1.44	.74 – 2.77
Functional limitations	1.19	.60 – 2.38	1.27	.73 – 2.21
Cognitive functioning	1.13	.77 – 1.66	.90	.70 – 1.16
Alcohol use	.69	.27 – 1.77	.57	.26 – 1.22
<i>Personality characteristics</i>				
Neuroticism	1.19	1.02 – 1.38	1.04	.93 – 1.16
Social Inadequacy	1.07	.93 – 1.24	.95	.84 – 1.07
Mastery	.84	.67 – 1.04	.85	.70 – 1.03
Self-efficacy	.93	.81 – 1.08	.78	.91 – 1.14
<i>Psychological symptoms</i>				
Severity of anxiety symptoms	1.15	.97 – 1.35	.98	.87 – 1.10
Depressive symptoms	1.05	.98 – 1.13	1.00	.95 – 1.06
<i>Social functioning</i>				
Emotional support	.76	.23 – 2.45	.36	.13 – 1.03
Loneliness	.91	.74 – 1.13	.99	.83 – 1.18
<i>Life changes</i>				
Level of distress	1.01	.99 – 1.03	1.00	.99 – 1.02
Increase in chronic diseases	.27	0.06 – 1.32	.81	.25 – 2.64
Increased functional limitations	1.03	.26 – 4.17	.46	.13 – 1.60
Cognitive decline	.00	.00 – 0.00	.67	.04 – 11.36

N.B. Odds ratios in bold typeface indicate a significantly higher chance
at persistent anxiety or partial remission

The results show that a lower socio-economic status was associated with partial remission of anxiety, but not with persistent anxiety. When controlling for differences in gender, the association between socio-economic status and partial remission was no longer significant. Sex, age and marital status were not associated with outcome of anxiety. None of the variables related to physical health, psychological symptoms, social functioning, treatment and life events were found to be associated with outcome of anxiety. Of the variables regarding personality characteristics, only neuroticism was related to the outcome of anxiety: a higher score on neuroticism at baseline was associated with a persistent outcome of anxiety, even when controlling for differences in age, gender, chronic diseases and severity of anxiety symptoms at baseline. Social inadequacy, mastery and self-efficacy were not associated with outcome of anxiety.

Mental health care service utilization and use of anxiolytic medication at follow-up.

In table 3, rates of mental health care service utilization and use of benzodiazepines and antidepressants at baseline and follow-up are presented. The use of benzodiazepines remained high for all groups, but was especially high for those with a persistent outcome of anxiety (43% vs. 21% for those in partial remission and 21% for those in full remission; $\chi^2 = 2.75$, ns), while use of antidepressants remained low (7% in those with a persistent outcome). A striking finding is that only 14% of those with a persistent outcome had been in recent contact with a mental health care practitioner.

Table 3. Health care service utilization of older people with an anxiety disorder at baseline

Health care service utilization (%)										
	Entire sample (n=62)				According to outcome of anxiety					
	At baseline (n=62)		At follow-up (n=62)		Persistent anxiety (n=14)		Partial remission (n=29)		Full remission (n=19)	
	n	%	n	%	n	%	n	%	n	%
Mental health care	9	15	3	5	2	14	1	3	0	0
Anti-depressants	4	7	4	7	1	7	1	3	2	11
Benzodiazepines	17	27	16	26	6	43	6	21	4	21

Discussion

In the present study we examined the outcome of anxiety disorders in older adults in the general population after a follow-up period of six years and we tried to identify prognostic factors for persistence of anxiety in older adults. As far as we know, this is the first study ever to investigate the long-term outcome of anxiety disorders in older adults. In light of previous findings on the low level of mental health care service utilization and the high level of benzodiazepine use in older adults with an anxiety disorder, this study also aimed to establish whether those with persistent anxiety were receiving appropriate care and medication.

The outcome of anxiety in older adults

23% of the older adults with an anxiety disorder at baseline who were available for follow-up met criteria for a persistent outcome six years after baseline measurement. Almost half (47%) of our sample met criteria for subsyndromal anxiety (the partial remission group), while approximately a third (31%) was in full remission of anxiety. Given the fluctuating course of anxiety disorders in younger populations (Reich, 1986), one should be careful not to put too much emphasis on the difference between a persistent outcome and a 'partial remission' outcome. In total, 69% of our sample suffered from either subsyndromal or full-blown anxiety at six-year follow-up, indicating a rather unfavorable outcome. However, the percentage for full remission is relatively high, considering that in studies with younger adults, full remission rates over a period of five to ten years range from 12 to 31% (Angst et al., 1991; Katschnig & Amering, 1998).

Our results suggest that anxiety disorders may have a different outcome than major depression in older adults. In contrast to our findings, rates for persistence have been found to be considerably higher for both major and minor depression in older adults than in mixed-age populations (Beekman et al., 2002).

Prognostic factors for a persistent outcome

Our results revealed only one predictor for a persistent outcome of anxiety: neuroticism. In a previous study by our research group, this personality trait had also been identified as a strong predictor for remaining anxious in late life (de Beurs et al., 2000) and there are a number of studies that have demonstrated an association between neuroticism and the onset and prognosis of mood and anxiety disorders (for an extensive review of these studies see Clark, Watson & Mineka, 1994). Although the OR found in our study (1.19) appears to be rather small, one should hold into account that neuroticism was entered into the analysis as a dimensional scale, which means that the OR is 1.19 for every one-point difference in scores on the neuroticism scale. One could argue that neuroticism is only found to be a predictor for a persistent outcome because it shows great conceptual overlap with anxiety. However, we found that neuroticism was still a strong predictor for a persistent outcome when controlling for the influence of severity of anxiety symptoms at baseline (OR=1.17, 95% confidence interval = [1.02-1.36]), which makes it highly unlikely that the overlap between anxiety and neuroticism is to be held accountable for this finding.

Also, in concordance with findings from community and general practitioner studies in mixed-age populations (Angst et al., 1991), female sex was not found to be related to persistence of anxiety. In some studies on the outcome of anxiety in mixed-age populations, stressful life events (Giel, ten Horn, Ormel, Schudel & Wiersma, 1978), the presence of comorbid medical disorders (Giel et al., 1978; Huxley, Goldberg, Maguire & Kincey, 1979), comorbid depression (Vollrath & Angst, 1989) and severity of illness (Woodman, Noyes, Jr., Black, Schlosser & Yagla, 1999) have been identified as prognostic factors for persistence of anxiety. None of these factors was related to persistence of anxiety in our sample of older adults. However, when looking at the raw data (see table 1) one could argue that certain prognostic factors for persistence of anxiety (such as female sex, low socio-economic status, severity of illness and stressful life events) failed to reach statistical significance due to small sample size (see section on 'limitations of the study' in this study).

Mental health care and anxiolytic medication

The use of benzodiazepines remains high for the entire group (26%), even in those in full remission of anxiety (21%), but is especially high in those with a persistent outcome (43%). In contrast, appropriate treatment for older adults suffering from anxiety remains disturbingly low: of those with a persistent outcome, only 7% used anti-depressants and 14% had been in recent contact with a mental health care facility. This implies that efforts to enhance appropriate referral of anxiety in older adults and to lower the use of benzodiazepines in this group in the Netherlands have not yet had the desired effect.

Limitations of the study

In any longitudinal research effort with respondents of old age, attrition rates are considerable and in our case, attrition due to death increased even further due to over-sampling of men and the 'older old'. Furthermore, a recent LASA publication shows that mortality rates were elevated in men (but not in women) with a diagnosed anxiety disorder (van Hout et al., 2004), which might also contribute to the high death rates in our sample. In order to establish whether selective attrition may have been a source of bias in the present study, we compared respondents lost to the follow-up assessment with those who were included on all relevant measures. Loss to follow-up was related to male sex; if anything, this may have led to an overestimation of the association between female sex and a persistent outcome. As we found no significant association between female sex and a persistent outcome, it is unlikely that the loss of male subjects biased our results. Furthermore, drop outs were older, less healthy and had a lower level of cognitive functioning at baseline measurement. Therefore, we may have failed to demonstrate the prognostic value of health-related factors for a persistent outcome of anxiety due to the loss of unhealthy subjects for follow up measurement. No differences between responders and drop outs were found on any of the other predictor variables, such as severity of anxiety and depressive symptoms, personality characteristics, socio-economic status or social functioning.

Our study sample included those with a comorbid depression ($n=29$, 26%). Excluding those with a comorbid depression may have rendered a clearer picture of the outcome of 'pure' anxiety disorders. However, it would also have limited generalizability of our findings since comorbidity with depression is typically high in anxious older adults (van Balkom et al., 2000). Another limitation to our study was the large time interval between measurements.

Unfortunately, no data were available for the outcome of anxiety at regular time intervals during the six-year follow-up, making it difficult to make any precise inferences on the course of anxiety in older people on the basis of our results.

Post-traumatic stress disorder, anxiety disorder not otherwise specified and mixed anxiety-depression were not included as anxiety disorders in the present study, while these might be common forms of anxiety in older adults.

Another shortcoming is that information regarding utilization of mental health care services was only available for a six-month period leading up to baseline and follow-up measurements. Respondents may have received treatment for anxiety in between measurements, which may in turn have influenced the outcome of anxiety at follow-up.

In this study, we tried to identify prognostic factors for a persistent outcome, partial remission or full remission of anxiety. One might argue that the difference between a persistent outcome and a partial or full remission could result from the absence of a single criterion in a diagnostic interview or the difference of one point on a screening instrument for anxiety. Therefore, multiple regression analyses were repeated on a dimensional scale for anxiety symptoms at follow-up, the HADS-A (Zigmond et al., 1983), while correcting for the influence of anxiety symptoms at baseline. Again, neuroticism was found to be the strongest prognostic factor for severity of anxiety symptoms at follow-up.

Concluding remarks

Our findings are indicative of a rather unfavorable long-term outcome of anxiety in older adults, with a substantial proportion meeting criteria for a persistent outcome after a follow-up period of six years. However, no conclusive inferences can be made on this subject, as follow-up data were restricted to only one point in time.

Neuroticism was found to be a strong prognostic factor for a persistent outcome of anxiety in later life. In future studies, it would be recommendable to ensure a larger sample size to be able to discern other prognostic factors for a persistent outcome of anxiety, as attrition rates are typically high in longitudinal research efforts with participants in the older age categories. Also, future longitudinal studies should entail observations regarding anxiety at regular time intervals, in order to firmly establish the course of anxiety in later life.

Despite several efforts in recent years to amplify the recognition and referral of anxiety disorders in later life, adequate treatment remains rare, while utilization of benzodiazepines remains high, especially in those with a persistent outcome of anxiety. Appropriate treatment may lead to a significant reduction of health care-related costs in anxious older adults.

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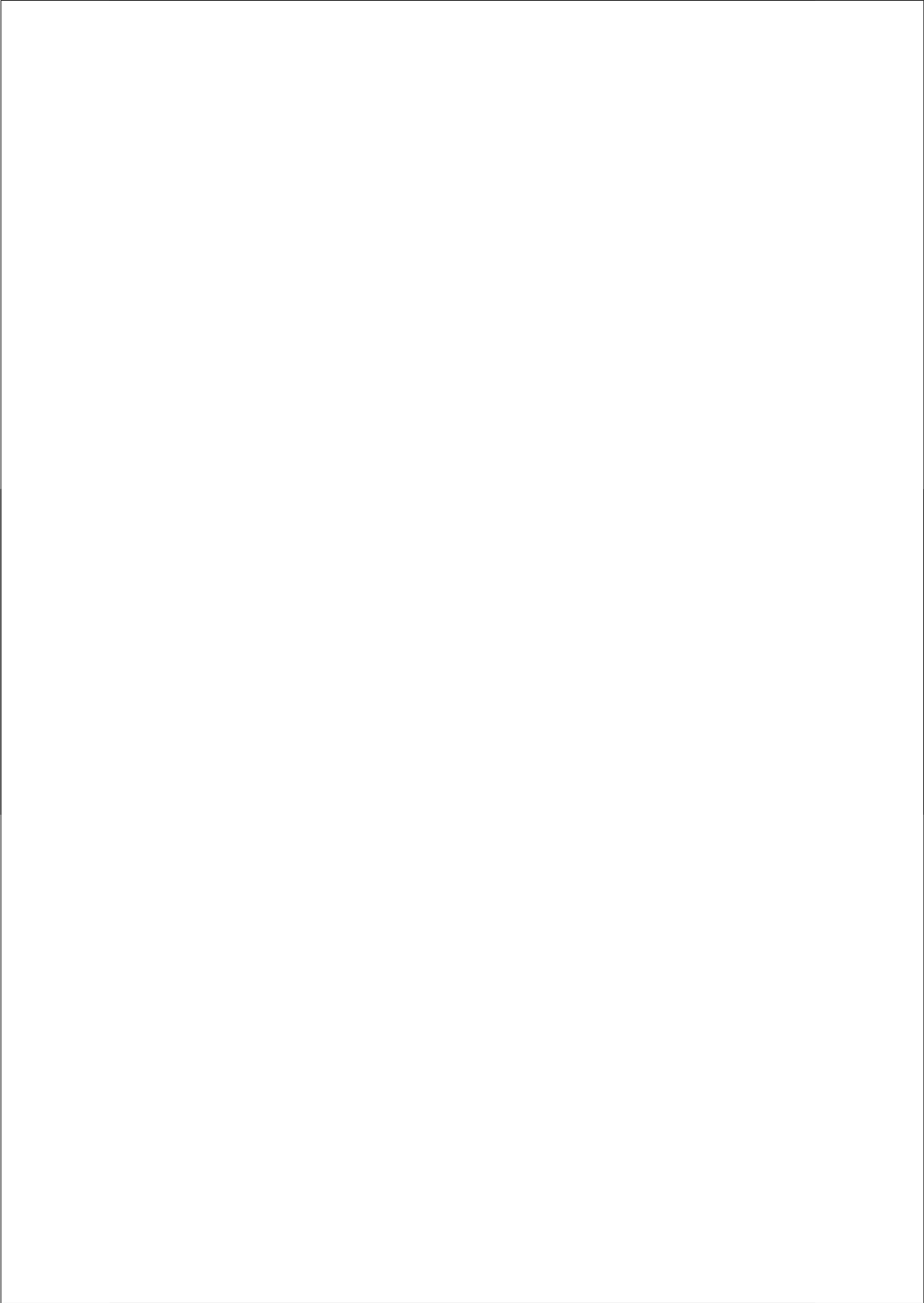
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Chapter 4



A randomized controlled trial of the effectiveness of cognitive-behavioral therapy and sertraline versus a wait-list control group for anxiety disorders in older adults.

Abstract

Objective: This study is the first to investigate the relative effectiveness of CBT compared to a SSRI (sertraline) in a RCT on the treatment of anxiety disorders in older adults.

Method: 84 patients of 60 years and over with a principal diagnosis of GAD, panic disorder, agoraphobia or social phobia were randomly assigned to one of three conditions: 15 sessions of CBT, pharmacological treatment with an SSRI (sertraline; maximum dosage 150mg) and a wait list control group. Participants completed measures of primary outcome (anxiety) and coexistent worry and depressive symptoms at baseline, post-treatment and at three-month follow-up. **Results:** Attrition rates were high in both treatment groups. Consequently, findings are based on a relatively small sample of completers ($n=52$). Although both CBT and sertraline led to significant improvement in anxiety, worry and depressive symptoms both at post-treatment and at three-month follow-up, sertraline showed superior results on worry symptoms. Effect size estimates for CBT were in the small to medium range, both at post-treatment (mean $d = .42$) and at three-month follow-up (mean $d = .35$), whereas effect sizes for sertraline fell into the large range (post-treatment mean $d = .94$ and three-month follow-up mean $d = 1.02$). The wait-list condition showed virtually no effects (post-treatment mean $d = .03$). **Conclusions:** Our findings strongly suggest that the pharmacological treatment of late-life anxiety with SSRIs has not been given the proper attention in research to date.

Schuurmans, J., Comijs, H.C., Emmelkamp, P.M.G., Gundy, C.M., Weijnen, I.J.C., van Hout, M.A., van Dyck, R. A revised version of this chapter has been accepted for publication by the American Journal of Geriatric Psychiatry.

Anxiety disorders are highly prevalent in older adults (Beekman et al., 1998) and are associated with increased disability, a great negative impact on quality of life (Wetherell et al., 2004) and an inadequate use of health care services and psychotropic medication (de Beurs et al., 1999). Hersen & van Hasselt (Hersen et al., 1992) have argued for the development of psychosocial interventions, because the prescription of benzodiazepines or even of safer psychotropic drugs such as selective serotonin reuptake inhibitors (SSRIs), might be problematic in older adults due to comorbidity with physical illness and potential negative interactions with other drugs. Although this is a valid argument, a pharmacological approach should not be discarded too hastily. In fact, randomized controlled trials of SSRIs in older adults with depression, although limited in number, have provided evidence for the effectiveness and tolerability of these drugs in older adults (Schneider et al., 2003), even in the 'older old' (Gildengers et al., 2002). Recently, the first randomized placebo-controlled trial evaluating the effectiveness of an SSRI (citalopram) in the treatment of late-life anxiety has been published (Lenze et al., 2005), providing preliminary evidence for the effectiveness and tolerability of this drug in anxious older adults. However, this study awaits replication in a larger sample.

Despite the argument for the development of psychosocial interventions for the treatment of anxiety in older adults, randomized controlled trials in this area are scarce. In mixed-age populations, empirical evidence suggests that cognitive behavioral therapy is the most effective form of psychotherapy for anxiety disorders (Emmelkamp, 2004). In recent years, several research efforts have been made, providing some evidence for the effectiveness of CBT in anxious older adults (Stanley et al., 2003a; Wetherell et al., 2003a; Barrowclough et al., 2001; Stanley et al., 1996), but the evidence is limited and not unequivocal (Mohlman, 2004).

Our study is one of the first to investigate the effectiveness of an SSRI (sertraline) in a randomized controlled trial of the treatment of anxiety disorders in older adults. Sertraline was chosen because it has been found to be effective and well tolerated, both in anxious mixed-age populations (McRae & Brady, 2001; Pohl, Wolkow & Clary, 1998; Allgulander et al., 2004; Liebowitz et al., 2003) and in depressed older

adults (Forlenza, Almeida, Stoppe, Jr., Hirata & Ferreira, 2001), even in case of comorbid medical illness (Sheikh et al., 2004). Also, in contrast to most research efforts in this area, our study will examine the effectiveness of individual rather than group CBT in anxious older adults and it will include other anxiety disorders than GAD, namely panic disorder, agoraphobia and social phobia. Furthermore, the current investigation is the first to compare CBT with a SSRI and a wait-list control group among older adults with an anxiety disorder. This study was approved by the Medical Ethical Review Board of the University Medical Centre of Maastricht.

Method

Participants

Participants included 84 adults, aged 60 years and over, with a principal Diagnostic and Statistical Manual of Mental Disorders (4th ed., American Psychiatric Association, 1994) diagnosis of GAD, panic disorder (either with or without agoraphobia), agoraphobia without a history of panic disorder or social phobia. Exclusion criteria were the presence of an organic condition that provided a contra-indication for the use of selective serotonin reuptake inhibitors, current use of antidepressant medication, a comorbid diagnosis of alcohol dependency, current participation in psychotherapy, a history of psychosis or cognitive impairment as indicated by clinical impression and a score of less than 26 on the Mini-Mental State Examination (Folstein, Folstein & McHugh, 1975a). Individuals stabilized on benzodiazepines were asked not to change their dose or type of medication for the duration of the study. Therapists were instructed to ensure that participants did not change their use of benzodiazepines. Individuals with comorbid depression, dysthymia, or other anxiety disorders were not excluded from participation, as long as their principal diagnosis was GAD, panic disorder, agoraphobia or social phobia. Principal diagnosis was defined as the most severely disabling disorder at the present time. Participants were recruited from 2000 to 2003 through media announcements, distribution of information leaflets in pharmacies and clinics for general practice and among referrals for treatment to community mental health centres and out-patient clinics in five cities in the western and southern part of the

Netherlands. All participants were selected on the basis of a structured diagnostic interview (SCID 2.0; First, Spitzer, Gibbon & Williams, 1999), administered by psychologists who had received extensive training in this instrument.

Over a 3.5 year recruitment period, 160 subjects received a diagnostic interview, of whom 115 people (72%) fit the inclusion criteria and were invited to participate in the research. Thirty-one patients (27%) refused before providing preliminary data. Eighty-four participants remained who were randomized into the study. Table 1 presents demographic and diagnostic information about the sample.

Table 1. Descriptives of the sample (prior to attrition)

Variable		CBT (n=42)	Sertraline (n=29)	Wait-list (n=13)	Total (n=84)
Age	M(SD)	70.71(6.58)	69.79(5.49)	66.85(5.96)	69.80(6.20)
Duration of anxiety (yrs)	M(SD)	23.33(23.46)	29.86(22.86)	27.22(25.52)	26.16(23.46)
Female	n (%)	31 (73.8)	22 (75.9)	9 (69.2)	62 (73.8)
Married	n (%)	23 (54.8)	18 (64.3)	6 (46.2)	47 (56.6)
Education					
Low	n (%)	19 (45.2)	12 (41.4)	5 (38.5)	36 (42.9)
Medium	n (%)	8 (19.0)	10 (34.5)	5 (38.5)	23 (27.4)
High	n (%)	15 (35.7)	7 (24.1)	3 (23.1)	25 (29.8)
Main diagnosis					
GAD	n (%)	14 (33.3)	10 (34.5)	5 (38.5)	29 (34.5)
Panic disorder ⁴	n (%)	17 (40.5)	16 (55.2)	5 (38.5)	38 (45.2)
Agoraphobia ⁵	n (%)	7 (16.7)	1 (3.4)	0 (0)	8 (9.5)
Social Phobia	n (%)	4 (9.5)	2 (6.9)	3 (23.1)	9 (10.7)
Comorbid diagnosis					
Specific phobia	n (%)	17 (40.5)	5 (17.2)	2 (15.4)	24 (28.6)
Other anxiety disorder	n (%)	22 (52.4)	11 (37.9)	5 (38.5)	36 (42.9)
Depression	n (%)	7 (16.7)	8 (27.6)	2 (15.4)	17 (20.2)

⁴ With or without agoraphobia

⁵ without a history of panic disorder

Procedures

All participants read and signed an informed consent form prior to being randomly assigned to one of three conditions: 15 weeks of CBT ($n=42$), sertraline ($n=29$) or a 15 week-waiting period ($n=13$). Randomization procedures were as follows: one envelope was filled with 62 labels stating 'CBT', 62 labels stating 'sertraline' and 26 labels stating 'wait-list'. Based on the assumption that the wait-list condition would show no effects, as is the case in comparable treatment studies (Wetherell et al., 2003), we planned for fewer subjects in the wait-list condition. This distribution would yield maximum power to detect differences between CBT and sertraline, while still allowing for enough power to differentiate between the active treatment conditions and the wait-list condition (Woods et al., 1998). When a participant had completed the screening procedure, the principal researcher would then blindly take one label out of the envelope which would then be excluded from further randomization procedures. However, even though we allowed for a lengthy recruitment period and great efforts were made to contact potential participants, we could only assign 84 participants and the remaining 66 labels were not used in the randomization procedure, which is why sample sizes are unequal.

Trained psychologists and a trained research assistant performed assessment interviews at pre-test and post-test and at three-month follow-up. Participants in the CBT condition were treated individually by a certified behavior therapist in 15 weekly one-hour sessions. CBT consisted of relaxation training, cognitive restructuring and exposure. Treatment protocols for CBT were derived from prevailing treatment protocols of panic disorder (Clark & Salkovskis, 1986), GAD (Borkovec & Costello, 1993) and social phobia (Scholing & Emmelkamp, 1995) in mixed-age populations which were adapted for use with older adults (our CBT protocol consisted of 15 sessions, allowing more attention to psycho-education and repeated explanation and revision of new information and newly learned coping skills). Participating therapists took part in regular supervision meetings, which were led by certified supervisors for behavior therapy (P.M.G. Emmelkamp and I.J.C. Weijnen). Although sessions were not taped and rated for adherence to the protocols,

therapists were repeatedly and explicitly instructed to contact their project supervisor if they felt that they needed to deviate from the protocol. Their supervisor would then talk through the problem at hand to ensure that therapists would adhere to the protocol.

In the sertraline condition patients were treated by a psychiatrist or a resident-psychiatrist in eight 20-minute sessions over a period of fifteen weeks. The protocol for sertraline included a dosage schedule adapted for older adults, in which the starter dose was lower (25 mg) and the dosage was built up more gradually than in the customary procedure (up to a minimum dose of 100 mg which had to be reached within four weeks and a maximum dose of 150 mg on the basis of tolerability and lack of clinical response). Medication was maintained during a three-month follow-up.

Measures

Outcome was assessed at post-treatment and at three-month follow-up. Pre and post-treatment measures consisted of self-report measures and a structured interview. The interview consisted of the Hamilton Anxiety Rating Scale (HARS; Hamilton, 1959; Cronbach's $\alpha = .82$). The HARS was performed by two members of the research group. Interrater agreement on the HARS was measured in the initial stages of the project. Weighted kappa was .58, constituting moderate interrater agreement. Self-report measures included the Beck Anxiety Inventory (BAI; Beck & Steer, 1990; Cronbach's $\alpha = .93$) and the Dutch adaptation of the Worry Domain Questionnaire (WDQ; Rijsoort, Emmelkamp & Vervaeke, 1999; Cronbach's $\alpha = .92$). Items related to work situations in the WDQ were omitted because they were not considered appropriate for an older population. Depressive symptoms were measured with the Centre for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977; Cronbach's $\alpha = .90$). The BAI and the HARS should be considered as the primary outcome measures of this study. Assessment at three-month follow-up consisted solely of self-report measures, which were distributed by mail, unless

participants preferred a personal interview with the researcher. In that case, questionnaires were handed out and filled in on site or taken home by the participant. Side effects to medication were measured with the Fawcett checklist (Fawcett, 1987) at the last session of the sertraline protocol.

Data Analysis

ANOVAs and chi-square tests were used to compare participants assigned to the three conditions on pre-treatment demographic and clinical variables, including number of coexistent diagnoses, number of chronic diseases and baseline anxiety measurements.

Therapy outcome was assessed with paired t tests and ANCOVAs on the outcome scores of both post-treatment and follow-up measurements using pre-treatment scores as a covariate (Gibbons et al., 1993). When outcome scores were missing, scores were imputed using scores from the next follow-up measurement if possible. When data were not normally distributed, wilcoxon signed rank tests were performed in stead of paired t tests. Two measures of clinically significant change were assessed: (1) Treatment response for anxiety, defined as an improvement of 20% on two measures of anxiety (BAI and HARS) and endstate functioning for anxiety, defined as a score of less than ten on both the BAI and the HARS (which equals a score within the normal range). The 20% reduction criterion of treatment response in a composite measure of both self-report and interview-rated instruments is frequently used in the treatment literature of anxiety in older adults (Wetherell et al., 2003; Barrowclough et al., 2001; Stanley et al., 1996). Rates of treatment response and endstate functioning were only available for post-treatment measurements.

Results

Attrition

Ten (12%) of 84 patients refused participation in the trial immediately after randomization, four of whom were assigned to sertraline, three to CBT and three to the wait-list condition. 17 (23%) of the remaining 74 participants dropped out of the trial before completing CBT (n=9), sertraline (n=7) or wait list conditions (n=1), culminating in a total attrition rate of 32% (27 of the initial sample of 84 participants). There were no significant differences in attrition rates across treatment groups. One participant randomized to sertraline switched to venlafaxine in one of the first weeks of treatment due to adverse side-effects and was excluded from outcome analysis. For completer analyses, data from 56 participants were available who completed CBT (n=30), sertraline (n=17) and wait-list conditions (n=9). Another four participants failed to turn in their pre-treatment questionnaires although they did complete the HARS interview, one of which was assigned to sertraline, two to CBT and one to the wait-list condition. Reasons mentioned for dropout from CBT included: Treatment was found to be too straining or confronting (n=2); treatment was found to be too time-consuming (n=2); participants did not agree with the treatment rationale (n=5) and spontaneous remission of symptoms (n=4). Reasons mentioned for dropout from sertraline included: long-term illness (n=1), deceased due to natural causes before starting medication (n=1), side-effects (n = 4), anticipated side-effects before actually starting medication (n=1) and spontaneous remission of symptoms (n=1).

No significant differences between dropouts and completers were found for sex, age, marital status, level of education, main psychiatric diagnosis, medication use, chronic illness or duration of symptoms. Non completers were found to have a higher score at pre-treatment on the HARS ($t=2.33$, $df=79$, $p < .05$), but not on any of the other outcome variables.

At three-month follow-up, four participants (9%) refused to fill in their questionnaires. During follow-up, three participants (two CBT and one sertraline participant) were given an alternative psychopharmacological treatment because their symptoms had not sufficiently improved. These participants were excluded from follow-up analyses, leaving a sample of 39 participants (25 CBT and 14 sertraline) who were included in follow-up analyses. Wait-list participants were not

included in follow-up analyses, as they were reassigned to one of the active treatment conditions after completing the 15-week waiting period.

Differences between therapy groups at pre-treatment

A comparison on all pre-treatment demographic and clinical variables, including the distribution of principal diagnosis and severity of anxiety symptoms at baseline using χ^2 tests and ANOVA's demonstrated no significant differences (table 1). After attrition, sertraline participants had a higher rate of comorbid depression at baseline than CBT or wait-list participants ($\chi^2 = 7.18(2)$, $p < .05$).

Treatment outcome

Paired t tests were performed to assess within-treatment effects for each group between pre-treatment and post-treatment and between pre-treatment and three-month follow-up. Results from wilcoxon signed rank tests showed the same results. Table 2 (page 85) presents t and p values, effect size estimates and percentage of change over time by condition.

At post-treatment, both CBT and sertraline participants had improved significantly on every outcome measure. Improvement was largely maintained during the three-month follow-up. Participants in the wait-list condition did not show significant change on any of the outcome measures. Effect size estimates were calculated as the difference between mean pre-and post-treatment scores divided by the pooled standard deviations from the baseline and post-treatment scores (Cohen's d ; Cohen, 1988). In general, effect sizes for CBT were in the small to medium range, both at post-treatment (mean $d=.42$) and at three-month follow-up (mean $d=.35$) whereas effect sizes for sertraline were in the large range (post-treatment mean $d=.94$ and three-month follow-up mean $d=1.02$). The wait-list condition showed virtually no effects (post-treatment mean $d=.03$).

At post-treatment, there were significant differences between CBT and WL on only one outcome measure; the HARS ($F=10.19(1, 35)$, $p<.01$). Sertraline performed better than WL on all outcome measures except the BAI (CES-D: $F=4.49(1,18)$, $p<.05$; HARS: $F=8.50(1, 22)$, $p<.01$; WDQ: $F= 4.44(1, 20)$, $p<.05$). In a comparison of the active treatment conditions, sertraline showed superior performance over CBT on the WDQ, but not on any of the other outcome measures, both at post-treatment, $F(1,41)=5.80$, $p<.05$ and at three-month follow-up, $F(1,35)=5.11$, $p<.05$.

Treatment response and endstate functioning

At post-treatment, 44% of CBT participants, 57% of sertraline participants and one wait-list participant (11%) could be classified as treatment responders. Separate χ^2 analyses of the three group comparisons revealed significant differences in treatment response rates between sertraline and wait-list ($\chi^2 = 4.87(1)$, $p<.05$), but not between CBT and wait-list ($\chi^2 = 3.25(1)$, $p=.08$) or between CBT and sertraline ($\chi^2 = .60(1)$, $p = .33$).

Prior to treatment, χ^2 analyses did not reveal any significant differences between conditions with regard to level of functioning for anxiety. Following treatment, 48% of CBT participants, 47% of sertraline participants and none of the wait-list participants fit criteria for high endstate functioning; $\chi^2 = 6.88(2)$, $p<.05$.

Adverse effects in the sertraline treatment group

Adverse effects that were reported by medication completers and that were deemed moderate to very severe by the (resident) psychiatrist at the last session of treatment were anorexia ($n=1$), tinnitus ($n=1$), stiffness ($n=1$), ataxia ($n=1$), dry mouth ($n=1$), hypertension ($n=1$), heart palpitations ($n=2$), miction problems ($n=2$), agitation ($n=2$), increase in appetite ($n=2$), tremors ($n=2$), nausea/vomiting ($n=2$), drowsiness ($n=2$), fatigue ($n=3$), headache ($n=3$), anxiety and nervousness ($n=3$), transpiration ($n=3$), insomnia ($n=3$), reduction of frequency of sex ($n=4$), problematic erection or

lubrication (n=4), absence of orgasm (n=4), lessened intensity of orgasm (n=4)
reduction of libido (n=5), depression (n=5) and pain (n=5).

Table 2. Paired t tests and p values, effect size estimates and percentage of change over time by condition

	CBT						Sertraline						Wait list					
	Pre-post-treatment (n=30)						Pre-treatment- 3 month follow-up (n=25)						Pre-post-treatment (n=17)					
	t	p	d	%	df		t	p	d	%	df		t	p	d	%	df	
BAI	3.47	<.01	.44	29	26		2.43	<.05	.36	25	23		3.98	<.01	.86	47	13	
CES-D	2.48	<.05	.31	18	26		2.06	.05	.34	17	23		3.66	<.01	.85	33	13	
HARS	4.39	<.01	.58	30	28				.96	43	15		4.30	<.01	.96	43	15	
WDQ	5.45	<.01	.36	14	27		2.89	<.01	.35	12	24		4.36	<.01	1.08	28	15	

d was calculated as $(M_{\text{pre-treatment}} - M_{\text{post-treatment}}) / \text{standard deviation}_{\text{pooled}}$

Discussion

Implications of our findings

Our study was the first to compare the effectiveness of a SSRI with CBT for the treatment of anxiety disorders in older adults. We found that although both treatments led to significant improvement on all measures of outcome, sertraline showed superior results on symptoms of worry as measured with the WDQ. Also, sertraline participants performed better than wait-list participants on 3 of 4 outcome measures, whilst CBT performed better than wait-list participants on only one outcome measure; the HARS. Moreover, effect sizes for CBT were relatively small (.31 -.58), while effect sizes for sertraline fell into the large range (.85 -1.08). However, treatment response rates and rates of high endstate functioning were not significantly different between treatment groups. Some of our findings run contrary to what one might expect on the basis of results from similar studies in mixed-age populations. In most RCT's of the treatment of anxiety disorders, SSRIs and CBT are found to be equally effective (Emmelkamp, 2004).

Our findings indicate that the reluctant attitude of both researchers and general practitioners toward the use of SSRIs in late-life may be unjustified. Given the fact that 4 participants (14%) did report side-effects as a reason for dropping out of the trial, which is comparable to dropout rates due to side-effects in studies of sertraline for depression in late life (11-19%; Sheikh et al., 2004; Bondareff et al., 2000; Newhouse et al., 2000), patients should be closely monitored and better informed on what to expect from an SSRI by their physician, in order to increase treatment adherence.

In concordance with most other treatment studies in late-life anxiety (Stanley et al., 2003; Wetherell et al., 2003; Stanley et al., 1996), effect sizes for CBT were substantially lower and attrition rates for both CBT and sertraline were considerably higher than those found in comparable treatment studies in mixed-age populations (mean attrition rate approximately 10%; Gould et al., 2004). These findings imply that it is important that we find ways to increase treatment adherence in older anxious adults.

CBT did not perform as well as expected on the basis of similar treatment studies in older adults. The only comparable trial that investigated individual format CBT in anxious older adults (with mixed anxiety disorders) was the study by Barrowclough et al. (2001), which yielded more positive results for CBT than our study. However, participants in Barrowclough's study were mostly treated in their own homes, which may have positively influenced both the effectiveness of treatment as well as treatment adherence. Also, 51% of participants in the Barrowclough study used antidepressants during the treatment phase, which may well have biased the results. Although treatment response rates were higher in the Barrowclough study (71% at 12-month follow-up), effect sizes for Barrowclough et al. (2001) were also in the small to medium range at .34. Also, participants in other treatment studies (Stanley et al., 2003; Wetherell et al., 2003; Stanley et al., 1996) were mostly well educated, while in our study 45% of CBT participants had only finished primary school.

Finally, problems with homework completion may play an important role in the moderate outcome of CBT in our study. Although we did not measure homework completion in a standardized manner, we do recall that one of the topics that came up frequently in our supervision meetings was the trouble that therapists encountered in getting participants to complete the homework. Reasons for this phenomenon were related to participants' disbelief in the usefulness of homework assignments, insecurity and difficulties in dealing with assignments and lack of time.

Limitations

The main limitation to the present study was its lack of power due to large attrition rates and the differences in sample size between conditions, which resulted from the fact that our randomization procedures were unsuccessful due to unforeseen recruitment problems. As a consequence, our study is not as persuasive as it might have been if other randomization procedures would have been used.

It should be taken into account that all outcome analyses in this study were based on completers. Due to high attrition rates and small sample size, no valid and meaningful way for performing intent-to-treat analyses was available.

Also, the follow-up period of this study was relatively short (three months), considering the fact that in mixed-age populations, the outcome of CBT tends to improve after termination of treatment (Gould et al., 2004). However, our results showed no improvement of CBT outcome during the three-month follow-up.

The fact that the use of sertraline was largely maintained during follow-up, may have biased the comparison with CBT, since evidence from younger populations suggests that anxiety symptoms tend to recur after termination of pharmacological treatment (Emmelkamp, 2004). Unfortunately, the Dutch review board for medical ethics did not grant us permission to allocate older adults to a placebo condition. As a consequence, we could not reliably establish whether treatment effect and reported side-effects should be attributed to sertraline. The fact that treatment in our study lasted for 15 weeks (more than twice the length of most pharmacological studies in younger populations) and the fact that treatment results were largely maintained during three-month follow-up, makes it less plausible that treatment effect is attributable to a placebo-effect.

Relating to the inclusion of different anxiety disorders, the fact that we chose not to include measures on phobic avoidance or the frequency of panic attacks might be considered as a limitation. However, such measures would not have been appropriate for all subjects, which is why we chose two outcome measures for general anxiety symptoms, the BAI and the HARS, as the main outcome measures of this study. Also, the inclusion of different anxiety disorders might limit the generalizability of our findings. The inclusion of agoraphobia without panic disorder in particular might induce comments on the fact that there is no specific evidence on the effectiveness of SSRIs for the treatment of this disorder. However, repeated outcome analyses excluding those with a main diagnosis of agoraphobia without panic disorder yielded similar results.

Finally, it should be noted that assessment was not blind and that follow-up assessments were solely based on self-report measures.

Recommendations and conclusions

Future randomized controlled trials might incorporate other psychological interventions that might be more suitable for use with older adults (such as reminiscence therapy which has shown positive results for the treatment of late-life depression (Bohlmeijer, Smit & Cuijpers, 2003)). Also, more research is needed to firmly establish if and what modifications are needed for the appropriate use of CBT with an older population. Finally, our findings strongly suggest that the pharmacological treatment of late-life anxiety with SSRIs has not been given the proper attention in research to date.

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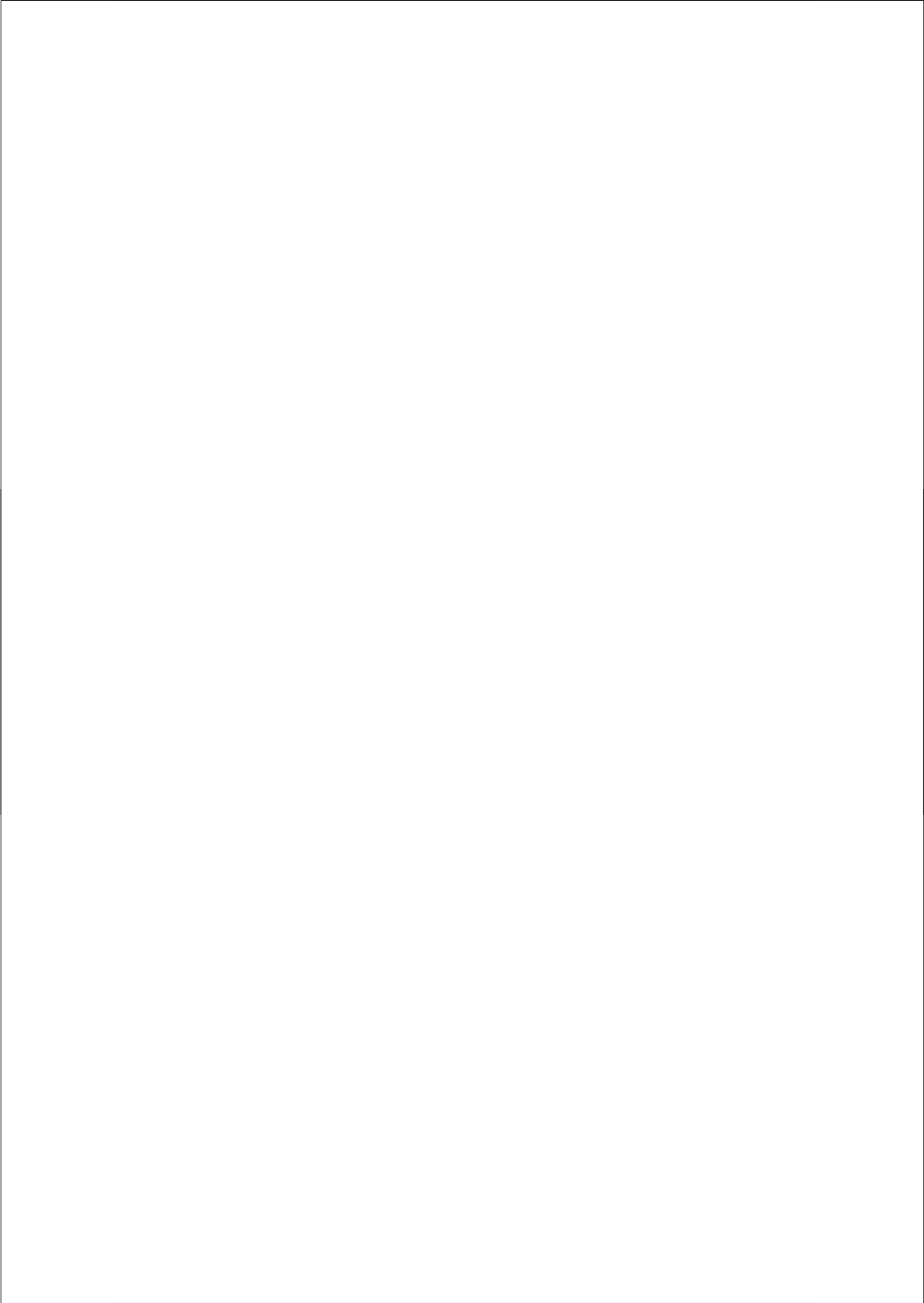
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Chapter 5



Long-term effectiveness and prediction of treatment outcome in cognitive behavioral therapy and sertraline for late-life anxiety disorders.

Abstract

Objective: The present study aims to establish long-term outcome of CBT and sertraline for the treatment of late-life anxiety and is the first to attempt to identify differential predictors for treatment outcome of sertraline and CBT for late-life anxiety disorders.

Method: Participants of an RCT comparing sertraline and CBT for the treatment of late-life anxiety were contacted one year after completing CBT and sertraline treatments, so that predictors for both short-term and long-term treatment outcome could be established.

Predictor variables included age, education, duration of symptoms, anxiety symptoms, depressive symptoms, agoraphobic symptoms, neuroticism and perceived health.

Results: Sertraline showed superior performance over CBT on anxiety (HARS) and worry (WDQ) ratings at one-year follow-up. A poor CBT outcome was predicted by poor perceived health, comorbid depressive symptoms and higher neuroticism scores. The strongest predictor for short-term CBT outcome was poor perceived health, explaining 40% of the variance in post-treatment residual gain scores on the HARS. The strongest predictor for long-term CBT outcome was neuroticism, explaining 20.0% of the variance in residual gain scores at one-year follow-up. Higher pre-test anxiety was found to be predictive of greater short-term improvement of anxiety symptoms in sertraline participants, explaining 41% of post-treatment residual gain scores. Analyses revealed no significant predictors for long-term treatment outcome in sertraline participants.

Conclusions: Our study suggests that sertraline might be more beneficial for late-life anxiety than CBT. Poor perceived health and neuroticism are predictive of less improvement after CBT in anxious older adults. Greater initial severity of anxiety seems to be predictive of a greater short-term treatment effect of sertraline in anxious older adults.

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This chapter has been submitted for publication.

Although anxiety disorders are among the most prevalent mental disorders among older adults (Flint, 1994b), randomized controlled trials of treatment effectiveness for late-life anxiety are scarce and have focused primarily on the effectiveness of psychotherapeutic interventions, more specifically: of CBT (Mohlman, 2004). Recently, our research group completed the first randomized controlled trial of the effectiveness of individual format CBT versus an SSRI (sertraline) for the treatment of late-life anxiety disorders (see chapter 4). Although both treatments resulted in statistically significant improvement in outcome scores, effect sizes for CBT were relatively small (post-treatment mean $d = .34$), whereas effect sizes for sertraline were in the large range (post-treatment mean $d = 1.00$). This is in concordance with a recent review of the treatment of late-life GAD (Mohlman, 2004), which concluded that effect sizes found in treatment studies of CBT for anxiety in older adults tend to be markedly lower than in similar studies in younger adults.

As yet, there have been no systematic studies investigating prognostic factors for the outcome of CBT for late-life anxiety. In mixed-age populations, studies on the prediction of treatment outcome for anxiety disorders are relatively scarce and often provide conflicting results. Documented predictors of the outcome of psychological interventions for anxiety in mixed-age populations include duration of illness (Scheibe & Albus, 1997), older age (Scheibe et al., 1997), initial severity of anxiety (Seivewright, Tyrer & Johnson, 1998; Butler, 1993), agoraphobic avoidance (Scheibe et al., 1997; Scheibe & Albus, 1996), pre-treatment depression (Scholing & Emmelkamp, 1999) and certain personality dimensions or disorders such as avoidant personality (Scholing et al., 1999). Documented predictors of the outcome of drug treatment for anxiety in younger and mixed-age populations seem to be similar to some extent, including such factors as symptom severity (Solvason, Ernst & Roth, 2003; Denys, Burger, van Megen, de Geus & Westenberg, 2003; Stein, Stein, Pitts, Kumar & Hunter, 2002), duration of symptoms (Solvason et al., 2003; Stein, Montgomery, Kasper & Tanghoj, 2001; Slaap & den Boer, 2001; Katschnig et al., 1995), depressive symptoms (Denys et al., 2003; Stein et al., 2001), agoraphobic avoidance (Slaap et al., 2001; Katschnig et al., 1995) and certain personality disorders or traits (Slaap et al., 2001).

Although these data suggest that the same factors may be of influence in determining treatment effect for CBT and psychopharmacological treatment, the evidence remains tentative as studies on differential predictors of treatment effect in comparative trials of psychological interventions versus drug treatments for anxiety are nonexistent. Also, not all findings from studies in mixed-age populations might be applicable to older adults, as treatment effectiveness studies of late-life anxiety have already proven. The different nature of both treatment modalities and the fact that we found some differences in degree of effectiveness between CBT and sertraline for the treatment of late-life anxiety calls for the study of differential predictors of treatment effect in this population.

The present study aims to establish long-term outcome of CBT and sertraline for the treatment of late-life anxiety and to identify differential predictors for treatment outcome of sertraline and CBT for late-life anxiety disorders. For the present study, participants of the original RCT were contacted and measured one year after completing CBT and sertraline conditions, so that predictors for both short-term and long-term treatment outcome could be investigated. Predictor variables included age, educational level, duration of symptoms, initial severity of anxiety, depressive symptoms, agoraphobic symptoms, neuroticism and perceived health.

Methods

The treatment study

Participants included 47 adults, aged 60 years and over, with a principal Diagnostic and Statistical Manual of Mental Disorders (4th ed.; American Psychiatric Association, 1994) diagnosis of GAD, panic disorder, agoraphobia (either with or without a history of panic disorder) or social phobia. Exclusion criteria were the presence of an organic condition that provided a contra-indication for the use of selective serotonin reuptake inhibitors, current use of antidepressant medication, a comorbid diagnosis of alcohol dependency, current participation in psychotherapy, cognitive impairment as indicated by a score of less than 26 on the Mini-Mental State

Examination (Folstein et al., 1975) or a history of psychosis. Individuals stabilized on benzodiazepines were asked not to change their dose or type of medication for the duration of the study. Individuals with comorbid depression, dysthymia, or other anxiety disorders were not excluded from participation, as long as their principal diagnosis was GAD, panic disorder, agoraphobia or social phobia.

All participants completed a fifteen-week CBT (n=30) or sertraline (n=17) treatment after randomized assignment to these conditions (see chapter 4). Measurements took place before and after completing treatment conditions, and at follow-up, one year post-treatment.

Age at pre-test varied from 61 to 81, with a mean age of 70. Age of onset was 'early' (below the age of 60) in 28 participants (59.6%) and duration of anxiety varied from 2 months to 63 years, with a mean duration of 29 years. Thirty-seven participants (78.7%) suffered from some form of chronic somatic disease. Chronic diseases that were most common among participants were hypertension (n=14; 29.8%), arthritis (n=10; 21.3%) and cardiovascular diseases (n=10; 21.3%). Twenty-three participants (48.9%) used one or more benzodiazepines. Further information regarding the distribution of descriptives across the treatment conditions can be found in table 1 (next page).

Measures of treatment outcome

Outcome was assessed at post-treatment and at one-year follow-up. Pre-test, post-test and follow-up measurements consisted of self-report measures and a structured interview. The interview consisted of the Hamilton Anxiety Rating Scale (HARS; Hamilton, 1959; Cronbach's $\alpha = .82$). The HARS was performed by two members of the research group. Interrater agreement on the HARS was measured in the initial stages of the project. Weighted kappa was .58, constituting moderate interrater agreement. Self-report measures included the Beck Anxiety Inventory (BAI; Beck et al., 1990; Cronbach's $\alpha = .93$) and the Dutch adaptation of the Worry Domain Questionnaire (WDQ; Rijsoort et al., 1999; Cronbach's $\alpha = .92$). Items related to

work situations in the WDQ were omitted because they were not considered appropriate for an older population. Depressive symptoms were measured with the Centre for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977; Cronbach's alpha= .90).

Table 1. Descriptives

Variable		CBT (n=30)	Sertraline (n=17)
Age at pre-test	M(SD)	70.60(6.52)	69.35(5.88)
Duration of symptoms (yrs)	M(SD)	27.85(25.20)	30.47(23.52)
Female	n(%)	21 (70.0)	12 (70.6)
Married	n (%)	17 (56.7)	13 (76.5)
Education			
Low	n (%)	14 (46.7)	5 (29.4)
Medium	n (%)	6 (20.0)	7 (41.2)
High	n (%)	10 (33.3)	5 (29.4)
Main diagnosis			
GAD	n (%)	8 (26.7)	7 (41.2)
Panic disorder ⁶	n (%)	14 (46.7)	8 (47.0)
Agoraphobia ⁷	n (%)	4 (13.3)	1 (5.9)
Social Phobia	n (%)	4 (13.3)	1 (5.9)
Chronic medical disorder	n (%)	26 (86.7)	11 (64.7)
Benzodiazepine use	n (%)	14 (46.7)	9 (52.9)
BAI pre-test	M(SD)	18.12 (11.92)	22.69 (13.60)
HARS pre-test	M(SD)	14.48 (8.00)	17.86 (8.22)
Depressive symptoms pre-test	M(SD)	19.59 (10.37)	23.78 (9.51)
Agoraphobic symptoms pre-test	M(SD)	36.50 (18.69)	37.03 (15.35)
Neuroticism pre-test	M(SD)	7.37 (3.32)	9.10 (2.36)
Perceived health	M(SD)	15.63 (5.54)	13.69 (4.81)

⁶ With or without agoraphobia

⁷ Without a history of panic disorder

Predictor variables of treatment outcome

Predictor variables of treatment outcome were measured at pre-test and included age, educational level, duration of symptoms in years, anxiety symptoms as measured with the BAI (Beck et al., 1990), depressive symptoms as measured with the CES-D; Radloff, 1977), agoraphobic symptoms as measured with the Agoraphobia Scale (AS; Ost, 1990; Cronbach's $\alpha = .96$), neuroticism as measured with the neuroticism subscale of the Eysenck Personality Questionnaire-revised, (EPQ-R; Eysenck et al., 1968; Eysenck et al., 1985; Cronbach's $\alpha = .78$) and perceived health (a subscale of the MOS-20; Stewart, Hays & Ware, Jr., 1988; Cronbach's $\alpha = .86$). Items related to driving a car were omitted from the analysis of the AS, since a large proportion of participants did not own or no longer owned a driver's license.

Data analysis

T tests and chi-square tests were used to compare participants assigned to CBT and sertraline on all predictor variables measured at pre-test. Therapy outcome at one-year follow-up was assessed with paired t tests and ANCOVAs on the outcome scores of follow-up measurements using pre-treatment scores as a covariate for all patients who completed treatment (Gibbons et al., 1993). Two measures of clinically significant change were assessed: (1) Treatment response for anxiety, defined as an improvement of 20% on two measures of anxiety (BAI and HARS) and high end state functioning for anxiety, defined as a score of less than ten on both the BAI and the HARS (which equals a score within the normal range). The 20% reduction criterion of treatment response in a composite measure of both self-report and interview-rated instruments is common in the treatment literature of anxiety in older adults (Wetherell et al., 2003a; Barrowclough et al., 2001; Stanley et al., 1996). Rates of treatment response and high end state functioning at one-year follow-up were determined and compared between treatment groups using χ^2 analyses.

Predictor analyses were conducted for two moments in time: at post-treatment and at one-year follow-up. To investigate the prognostic value of predictor variables measured at pre-test for treatment outcome of anxiety, residual gain scores (Steketee & Chambless, 1992) were used for the HARS, which was chosen as the main outcome variable. The residual gain score has several advantages over raw outcome scores or change scores, because it takes into account both pre-treatment differences and measurement error, by using the following formula: $\text{residT2} = z2 - z1 * r12$ (residT2 is the residual gain score at post-test (T2); $z2$ is the standardized score at post-test(T2); $z1$ is the pre-treatment standardized score, and $r12$ is the correlation between $z1$ and $z2$). A series of linear regression analysis were run, using residual gain scores on the HARS at post-treatment and follow-up as outcome variables. Data for CBT and sertraline completers were analyzed separately. First, all predictor variables were entered individually in a univariate linear regression model. Next, all predictors showing a significant effect in the univariate regression analyses were entered in a forward multivariate regression model, to see which of the variables showed an independent contribution to treatment outcome and to establish the magnitude of this contribution (the amount of variance in residual gain scores explained).

Results

Loss to follow-up and differences between treatment groups

For post-treatment analyses, data from 47 participants were available who completed CBT ($n=30$) and sertraline ($n=17$) conditions. Eight participants refused to cooperate with assessment at one-year follow-up, leaving a sample of 39 (25 CBT and 14 sertraline) participants who were included in follow-up analyses. Those who were lost to follow-up scored lower on the perceived health scale at baseline than those who participated in one-year follow-up assessments ($t(42)=2.09$, $p<.05$). No other significant differences between participants and those lost to follow-up were found for any of the demographic or predictor variables included in this study. Also, ANCOVA's on the post-treatment outcome measures using pre-treatment scores as a covariate did not show differences in treatment effectiveness between participants

and those lost to follow-up. Sertraline use was maintained during follow-up in at least 7 of 14 participants (50%). Unfortunately, data on sertraline use during follow-up are missing in 4 of 14 participants (28.6%). During follow-up, 7 participants (3 CBT and 4 sertraline participants) sought additional treatment at the research centre, 4 of which received an alternative psychopharmacological treatment and 3 of which received CBT.

A comparison on all pre-treatment demographic and predictor variables using t tests and χ^2 tests demonstrated no significant differences between those randomized to CBT or sertraline at baseline. However, sertraline completers did have a higher rate of comorbid depression at baseline than CBT completers (44.4 versus 10.0 %; $\chi^2(1)=7.56, p<.05$).

Treatment outcome at one-year follow-up

Paired t tests were performed to assess within-treatment effects for each group between pre-treatment and one-year follow-up. Table 2 presents t and p values, effect size estimates and percentage of change over time by condition.

Table 2. Paired t tests (t), effect size estimates (d) and percentage of change over time(%)

	CBT (n=25)					Sertraline (n=14)				
	Pre-treatment- 1-yr follow-up					Pre-treatment- 1-yr follow-up				
	t	p	d	%	df	t	p	d	%	df
BAI	1.92	.07	.28	19	23	4.01	<.01	.60	38	12
HARS	4.42	<.001	.70	34	24	5.18	<.001	1.62	62	13
CES-D	1.07	.30	.22	12	23	3.15	<.01	.82	29	12
WDQ	3.18	<.01	.27	10	24	4.12	<.01	.95	23	12

At one-year follow-up, improvement from baseline scores was significant on all outcome measures for sertraline completers. For CBT completers, improvement from

baseline scores was significant on the HARS and the WDQ, but not on the BAI or the CES-D. Effect size estimates were calculated as the difference between mean pre-and one-year follow-up scores divided by the pooled standard deviations from baseline and follow-up scores (Cohen's d ; Cohen, 1988). In general, effect sizes for CBT at one-year follow-up remained relatively small (mean d at one-year follow-up=.37 versus post-treatment mean d = .42 and three-month follow-up mean d = .35 (see chapter 4), whereas effect sizes for sertraline remained in the large range (one-year follow-up mean d = 1.00 versus post-treatment mean d = .94 and three-month follow-up mean d = 1.02).

For a direct comparison of the effectiveness of treatment conditions, we conducted ANCOVAs on the follow-up scores of all completers with pre-treatment scores as the covariate. Results favored sertraline on the HARS ($F_{(1,37)} = 5.54$, $p < .05$) and the WDQ ($F_{(1,36)} = 5.35$, $p < .05$), but not on the BAI ($F_{(1,35)} = 2.02$, $p = .16$) and the CES-D ($F_{(1,35)} = .62$, $p = .44$). At post-treatment, rates of treatment response (57% for sertraline versus 44% for CBT participants) and high end state functioning (47% for sertraline and 48% for CBT participants) did not differ significantly between treatment groups (see chapter 4). At one-year follow-up, 67% of sertraline participants and 39% of CBT participants could be classified as treatment responders ($\chi^2(1) = 2.39$, $p = .12$). Fifty-seven percent of sertraline participants and 44% of CBT participants fit criteria for high end state functioning at one-year follow-up ($\chi^2(1) = .62$, $p = .43$).

Predictors of treatment outcome for CBT

Regression analyses on post-treatment scores of the HARS using pre-treatment scores on the HARS as an independent variable revealed that 57.3% of the variance in post-test scores on the HARS was explained by the pre-test ($\beta = .77$, $p < .001$). Regression analyses on residual gain scores at post-treatment revealed several significant predictors for an unsuccessful treatment outcome for CBT participants. These included comorbid depressive symptoms, neuroticism and lower perceived health scores (table 3). A multiple forward regression analyses incorporating these

predictors revealed that only lower perceived health had a significant independent contribution to the prediction of an unsuccessful treatment outcome ($\beta = -.63$, $p < .01$), explaining 40.0% of the variance in residual gain scores.

At one-year follow-up, 45.3% of the variance in HARS scores was explained by the pre-test scores ($\beta = .69$, $p < .001$). Regression analyses on residual gain scores at one-year follow-up again revealed lower perceived health and neuroticism as significant predictors for an unsuccessful treatment outcome (table 3). Comorbid depressive symptoms were not found to be predictive for long-term treatment outcome. In contrast to post-treatment analyses, a multiple forward regression analyses incorporating perceived health and neuroticism revealed that only neuroticism had a significant independent contribution to the prediction of an unsuccessful treatment outcome at one-year follow-up ($\beta = -.63$, $p < .01$), explaining 22.0% of the variance in residual gain scores.

Predictors of treatment outcome for sertraline

Regression analyses on post-treatment HARS scores using pre-treatment scores as an independent variable revealed that 36.5% of the variance in post-treatment HARS scores was explained by the pre-test ($\beta = .60$, $p < .05$). Residual gain score analysis at post-treatment revealed one significant predictor of treatment effect; a higher pre-test anxiety score (as measured with the BAI) predicting more improvement (explained variance 41%, $\beta = .64$, $p < .05$).

Regression analyses on HARS scores at one-year follow-up revealed that only 13% of the variance in follow-up HARS scores was explained by the pre-test ($\beta = .36$, $p = .20$). Regression analyses on residual gain scores at one-year follow-up revealed no significant predictors for treatment outcome.

Table 3. Predictors of post-treatment and one-year follow-up residual gain scores on the HARS for CBT and sertraline participants.

Predictor variables	Post-treatment			1-year follow-up		
CBT	r ²	β	p	r ²	β	p
Age at pre-test	.11	.34	.07	.10	.31	.13
Educational level	.02	-.12	.53	.01	-.11	.62
Duration of symptoms	.00	.03	.88	.00	-.04	.87
Anxiety symptoms (BAI)	.05	.23	.24	.13	.35	.09
Depressive symptoms	.21	.46	<.05	.07	.26	.22
Agoraphobic symptoms	.01	.11	.57	.04	.20	.36
Neuroticism	.26	.51	<.01	.22	.47	<.05
Perceived health	.40	-.63	<.001	.18	-.43	<.05
Sertraline						
Age at pre-test	.00	.07	.79	.03	.19	.53
Educational level	.03	-.18	.50	.01	.08	.78
Duration of symptoms	.06	-.25	.36	.02	-.13	.68
Anxiety symptoms (BAI)	.41	.64	<.05	.13	.34	.23
Depressive symptoms	.00	.06	.84	.01	-.09	.76
Agoraphobic symptoms	.09	.29	.31	.03	.17	.56
Neuroticism	.00	.00	.99	.00	.01	.98
Perceived health	.05	-.22	.45	.01	-.10	.76

Regression analyses in bold typeface represent significance at $p < .05$

Discussion

Treatment outcome at one-year follow-up

Data comparing short-term effectiveness of CBT and sertraline for late-life anxiety, described in a previous report by our research group (see chapter 4), revealed higher effect sizes and a better result on worry symptoms for sertraline. Long-term treatment outcome reflects similar results with sertraline showing more improvement on worry symptoms, but also on anxiety symptoms as measured with the HARS. Effect sizes for sertraline remained in the moderate to large range

(Cohen's $d = .60 - 1.62$), while effect sizes for CBT were small to moderate (Cohen's $d = .22 - .70$).

Variables predicting treatment response

Our study provides support for several predictors for the treatment outcome of CBT for late-life anxiety, including comorbid depressive symptoms, poor perceived health and neuroticism. Poor perceived health seems to be predictive for treatment failure in CBT, but not in sertraline participants. This is a rather remarkable finding, since several papers have argued that psychological interventions are preferential to drug treatment for late-life anxiety (Mohlman, 2004; Nordhus et al., 2003; Hersen et al., 1992), because poor health is supposed to be detrimental to drug treatment effect in older adults. Neuroticism was found to be the strongest predictor for an unsuccessful long-term treatment outcome. Neuroticism has also been found to be predictive of a natural long-term persistent outcome of anxiety disorders in late-life (see chapter 3; Schuurmans et al., 2005) and it has been found to be related to the onset and prognosis of mood and anxiety disorders in mixed-age populations in several other studies (for an extensive review of these studies see Clark et al., 1994). Higher pre-test anxiety was found to be predictive of greater short-term improvement of anxiety symptoms in sertraline participants. Unfortunately, we were not able to discern any predictors for long-term treatment outcome in sertraline participants. Some of the documented predictors of treatment effect found in mixed-age populations, such as duration of symptoms for both CBT and pharmacological treatment outcome (Solvason et al., 2003; Slaap et al., 2001; Stein et al., 2001; Scheibe et al., 1997; Katschnig et al., 1995), and depressive symptoms for pharmacological treatment outcome (Denys et al., 2003; Stein et al., 2001) were not found to be related to outcome in our study. It should be noted however, that some of the analyses reported in this study may have failed to reach statistical significance due to small sample size (see section on 'limitations').

Limitations

The main limitation to the present study was its lack of power due to small sample size, differences in sample size between treatment conditions (see chapter 4) and loss of subjects for follow-up measurements. As a consequence, certain predictors of treatment effect may have been overlooked.

Although treatment results for sertraline in this study seem promising, it should be held into account that all analyses in the present study were based on completers and that the use of sertraline was maintained during follow-up in at least 50% of sertraline participants, which may have biased the comparison with CBT. Furthermore, since the review board for medical ethics did not grant us permission to allocate older adults to a placebo condition, we can not be certain if treatment effect should be solely attributed to the use of sertraline. However, the fact that treatment results were maintained during a one-year follow-up period makes it less plausible that treatment effect is attributable to a placebo-effect (Quitkin et al., 1987).

No significant predictors of long-term sertraline treatment effect were found in this investigation. However, some of the predictors of drug treatment effect reported in studies in mixed-age populations were not included in the present study, such as the presence of certain early side effects (Solvason et al., 2003) and unfamiliarity with psychopharmacological treatment (Solvason et al., 2003; Stein et al., 2001). Also, the sertraline group was markedly smaller than the CBT group, resulting in a substantial difference in statistical power to detect possible predictors of treatment effect between the two conditions.

Finally, it should be noted that participants were not requested to refrain from seeking additional treatment during follow-up and seven participants received additional treatment during follow-up at one of our research centres, which may have biased our results.

Recommendations and conclusions

Long-term outcome analyses of the present study suggest that sertraline might be more beneficial for the treatment of late-life anxiety than CBT. Our results clearly call for more studies on the pharmacological treatment of late-life anxiety with SSRIs, involving larger samples and a placebo condition to establish true drug response. For anxious older adults, the barrier to seeking psychotherapeutic treatment from a mental health care specialist is high, due to logistic problems (e.g. transportation), the psychological strain involved in psychotherapy and the stigma on psychiatric care for this generation. Drug treatment with SSRIs may provide a solution to this problem, as in most cases the medication can be prescribed by the general practitioner. However, for those anxious older adults who are reluctant to take medication or who have a somatic disease that provides a contra-indication for the use of SSRIs, psychological interventions are necessary. Short-term psychological interventions provided in a primary care setting may be more cost-effective and moreover, more accessible to this particular group, than a relatively long and straining cognitive behavioral treatment in a psychiatric setting. One study provides limited support for a short-term CBT intervention for late-life anxiety in primary care (Stanley et al., 2003b), but more research is needed to develop effective primary care interventions for this population.

Poor perceived health and neuroticism seem to be predictive of CBT treatment failure in anxious older adults. Greater initial severity of anxiety seems to be predictive of a greater short-term treatment effect of sertraline in anxious older adults. Future comparative treatment studies of CBT and SSRIs for late-life anxiety should include other possible predictors of treatment effect, such as the presence of certain (early) side effects, unfamiliarity with drug treatment, comorbid medication use and medical conditions. This could provide more cues for clinical practice to establish the preferred type of treatment for a certain individual.

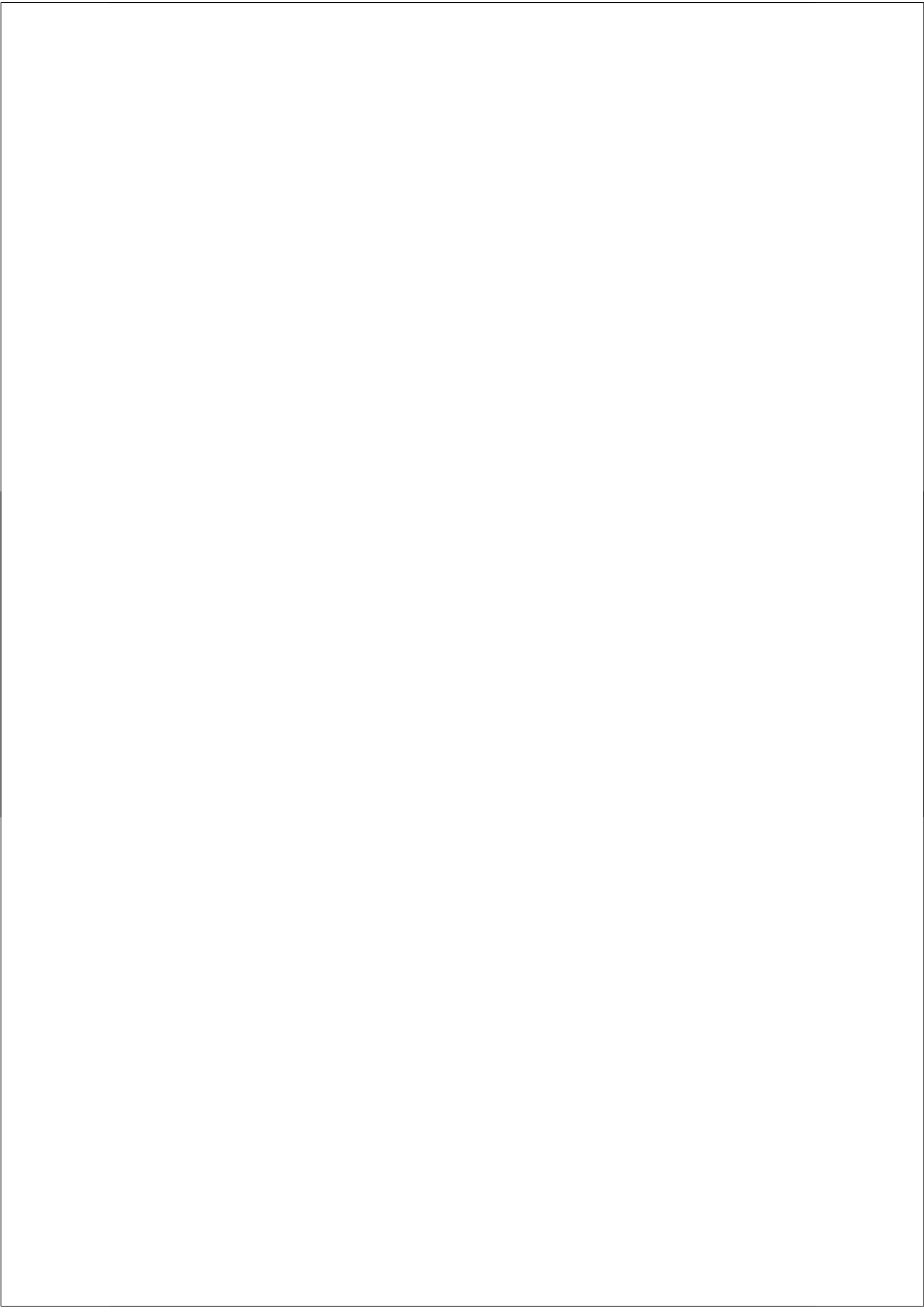
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Chapter 6



Attrition and recruitment in a late-life anxiety treatment study.

Abstract

Objective: To study variables related to acceptability of treatment and to investigate a possible bias in treatment studies of late-life anxiety as a result of high attrition rates and the recruitment of participants from the general population. **Method:** Data from a randomized controlled trial of CBT versus sertraline for late-life anxiety were used to analyze differences between treatment refusers and dropouts versus completers and between recruited and clinically referred participants. **Results:** CBT dropouts were found to have a higher neuroticism score and a higher rate of comorbid depression at baseline than CBT completers, whilst sertraline dropouts showed lower rates of comorbid depression than sertraline completers. Recruited participants were found to be more educated and less severely impaired, both physically and mentally, than referred participants. **Conclusions:** Recruitment of participants from the general population may lead to a selection bias of relatively healthy subjects for late-life anxiety treatment studies. SSRIs may be more acceptable to anxious older adults with comorbid depression whilst CBT might be more appropriate to those low in neuroticism and without a comorbid depression.

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Treatment studies of late-life anxiety (Stanley et al., 2003a; Stanley et al., 1996; Wetherell et al., 2003a) tend to have two characteristics in common: high attrition rates and a painstaking recruitment process, which is often largely accomplished through media announcements (Akkerman et al., 2001; Wetherell et al., 2001). The fact that both characteristics carry a risk for potential bias of research findings is a disregarded area in the literature on late-life anxiety treatments.

Reported dropout rates in CBT treatment studies of late-life anxiety vary from 23% to 33% (Stanley et al., 2003a; Stanley et al., 1996; Wetherell et al., 2003a), whereas reported dropout rates in similar treatment studies in mixed-age populations center around 10% (Gould et al., 2004). High attrition poses a problem for treatment studies of late-life anxiety in two ways: 1) It affects the validity and generalizability of results from treatment studies; 2) it has serious implications for the effectiveness of treatment of late-life anxiety in everyday practice, for what good is any given treatment if approximately a quarter to a third of your target population will not even complete treatment? It is important to take into account here that attrition rates in non-trial settings may be even higher, since researchers tend to put more effort into retaining patients for their study than a therapist would do in a 'normal' psychotherapeutic setting. Hunt and Andrews (1992) suggest that the dropout rate in treatment studies may not be attributable to patient characteristics, but should instead be viewed as a performance indicator of the treatment. They claim that dropout rates might be related to treatment factors, such as the level of effectiveness and efficiency (level of structure, time-limits) of the treatment given. In concordance, a meta-analysis of dropout in psychological outreach programmes for depressed older adults found that the dropout rate was particularly high in cognitive behavioral therapies when compared to several other interventions (including behavior therapy, psychodynamic therapy, bibliotherapy). The dropout rate was also higher in group interventions when compared to individual interventions and in lengthier versus shorter interventions (Cuijpers, 1998). In any case, dropout rates can be viewed as a measure of how acceptable a given treatment is to a particular group and in that respect, the performance of CBT for late-life anxiety leaves much to be desired. It has been suggested that logistic problems (e.g. transportation), resulting

from a higher prevalence of poor health and disability among older adults, are responsible for the differences in attrition rates between treatment studies of anxiety in younger versus older adults (Stanley et al., 2003), but this hypothesis awaits scientific testing. Poor health has been found to be related to dropout in one study of attrition in a mixed-age outpatient clinic for anxiety disorders (Issakidis et al., 2004).

With respect to the treatment of late-life anxiety with SSRIs, data on effectiveness and attrition rates are scarce. Researchers and clinicians have advocated the development of psychotherapeutic interventions (Nordhus et al., 2003; Hersen et al., 1992), because SSRIs might not be well-tolerated by older adults, especially in case of somatic comorbidity. It would be interesting to investigate whether physical health is indeed related to early termination of pharmacological treatment in older adults. Recently, the authors of the present study completed the first randomized controlled trial of cognitive behavioral therapy (CBT) versus an SSRI (sertraline) for the treatment of anxiety in older adults. Although dropout rates did not differ significantly between the two treatment conditions, dropout rates were marginally higher for sertraline (28%) than for CBT (23%). Seventeen percent ($n=5$) of participants originally randomized to sertraline reported adverse side effects as a reason for dropping out of the trial.

In order to become aware of a possible bias in treatment studies of late-life anxiety and to develop avenues for improving treatment adherence in anxious older adults, it is vital to know why people drop out of treatment and what characteristics set them apart from completers. Until now, no systematic study has been undertaken to this effect. Furthermore, determining differential characteristics of CBT dropouts and SSRI dropouts might also provide us with information on which treatment is more acceptable to which type of patient.

Another possible bias lies in the fact that most available treatment studies of late-life anxiety e.g. (Stanley et al., 2003; 1996; Wetherell et al., 2003a) actively recruited a large proportion or all of their participants through media announcements. Recruitment among referrals from mental health care centres is problematic, because anxious older adults are rarely appropriately referred and even when they are,

anxiety disorders often go unrecognized (Akkerman et al., 2001; Wetherell et al., 2001). However, the fact that most participants of treatment studies of late-life anxiety are actively recruited by the researchers does endanger the generalizability of results. Some have argued that actively recruited participants might not define themselves as needing psychiatric help (Covi, Lipman, McNair & Czerlinsky, 1979), which might in turn affect motivation for treatment. Available data on this subject, although scarce and contradictory, suggest that active recruitment of subjects for clinical outcome studies might lead to considerable bias. Comparative studies between solicited and nonsolicited (mixed-age) populations in mental health treatment trials have reported pre-treatment symptomatology differences, demographic differences, differences in past psychiatric treatment, differences in illness duration and differences in attrition rates (Rapaport et al., 1996; Aronson, 1987; Krupnick et al., 1986).

The present study uses data from a randomized controlled trial of CBT versus sertraline for late-life anxiety (see chapter 4) in order to investigate a possible bias in treatment studies of anxious older adults by determining the characteristic features of dropouts versus completers and of recruited versus clinically referred patients from mental health care centres in the treatment of late-life anxiety. Emmelkamp and van der Hout (1983) have made a distinction between nonacceptance (a refusal to start the treatment offered) and dropout during treatment. Most studies tend to disregard nonacceptance in their attrition analyses, stating that those who refuse treatment are different than treatment dropouts. Although this might be true, both treatment refusal and early termination of treatment can be regarded as a type of treatment failure (Emmelkamp et al., 1983) and it is well worth investigating whether and how treatment refusers are different from those who complete treatment and those who drop out of treatment. Therefore, treatment refusers are included in the present study as a separate group. However, results from these analyses should be interpreted with caution as treatment refusers constitute a very small subsample ($n=3$ in the CBT and $n=4$ in the sertraline condition).

Method

Sample

Over a 3.5-year recruitment period, 160 older adults (aged 60 years and over) received a diagnostic interview, of whom 115 people (72%) fit the inclusion criteria and were invited to participate in a randomized controlled trial of CBT versus sertraline and a wait-list control group. Thirty-one patients (27%) refused before providing preliminary data. Eighty-four participants remained who read and signed an informed consent form prior to being randomly assigned to CBT ($n=42$), sertraline ($n=29$) and wait-list ($n=13$). Sample sizes are unequal because 1) we planned for fewer subjects in the wait-list condition and 2) we planned for 150 subjects in our randomization procedures, but despite great efforts to contact participants for the study, unfortunately we were unable to reach these numbers (see chapter 4 for more details on the randomization procedures). Participants included 84 adults, aged 60 years and over, with a principal Diagnostic and Statistical Manual of Mental Disorders (4th ed., American Psychiatric Association, 1994) diagnosis of panic disorder (either with or without agoraphobia) ($n=38$; 45.2%), GAD ($n=29$; 34.5%), social phobia ($n=9$; 10.7%) or agoraphobia without a history of panic disorder ($n=8$; 9.5%). Exclusion criteria were the presence of an organic condition that provided a contra-indication for the use of selective serotonin reuptake inhibitors, current use of antidepressant medication, a comorbid diagnosis of alcohol dependency, current participation in psychotherapy, a history of psychosis or cognitive impairment as indicated by clinical impression and a score of less than 26 on the Mini-Mental State Examination (Folstein et al., 1975). The presence of comorbid depression, dysthymia, or other anxiety disorders was not a basis for exclusion from the study, as long as the principal diagnosis was GAD, panic disorder, agoraphobia or social phobia. Principal diagnosis was defined as the most severely disabling disorder at the present time. Participants were recruited from 2000 to 2003 through various types of media announcements (articles in regional newspapers, interviews broadcasted on radio and television), distribution of information leaflets in pharmacies and clinics for general practice (the actively recruited participants) and among referrals for treatment to community mental health centres and out-patient clinics in five cities in the western and southern part of the Netherlands (the clinically referred

participants). All participants were selected on the basis of a structured diagnostic interview (SCID 2.0; First et al., 1999), administered by psychologists who had received extensive training in this instrument.

Participants were predominantly female (n=62; 73.8%) and 47 participants were married (56.0%). Age at entering the treatment study ranged from 61 to 83 years, with a mean age of 69.8 years. Age of onset of anxiety was 'late' (at or after the age of 60) in 29 cases (34.5%). Duration of anxiety ranged from two months to 63 years, with a mean duration of 26 years. Thirty-three participants (39.3%) were clinically referred to one of the participating mental health care centres, 51 participants (60.7%) responded to media announcements or information leaflets. Sixty-seven participants (79.8%) suffered from some form of chronic disease. Chronic diseases that were most common among participants were hypertension (n=28; 33.3%), cardiovascular diseases (n=19; 22.6%) and arthritis (n= 28, 33.3%). Forty-one participants (48.8%) used one or more benzodiazepines. Comorbid psychiatric diagnoses consisted mainly of specific phobia (n=24; 28.6%), other anxiety disorders (n=36; 42.9%), and depression (n=17; 20.2%).

Ten (11.9%) of 84 patients refused participation in the trial immediately after randomization, four of whom were assigned to sertraline, three to CBT and three to the wait-list condition. Another 17 participants (20.2%) dropped out of the trial before completing CBT (n=9), sertraline (n=7) or wait list conditions (n=1), culminating in a total attrition rate of 32% (27 of the initial sample of 84 participants). There were no significant differences in attrition rates across treatment groups. Reasons mentioned for dropout from CBT included: Treatment was found to be too straining or confronting (n=2); treatment was found to be too time-consuming (n=2); participants did not agree with the treatment rationale (n=5) and spontaneous remission of symptoms (n=4). Reasons mentioned for dropout from sertraline included: long-term illness (n=1), deceased due to natural causes before starting medication (n=1), side-effects (n = 4), anticipated side-effects before actually starting medication (n=1) and spontaneous remission of symptoms (n=1) (see chapter 4).

The treatment conditions

Participants in the CBT condition received 15 weekly individual one-hour sessions by a certified behavior therapist. CBT consisted of relaxation training, cognitive restructuring and exposure. Treatment protocols for CBT were derived from prevailing treatment protocols of panic disorder (Clark et al., 1986), GAD (Borkovec et al., 1993) and social phobia (Scholing et al., 1995) in mixed-age populations which were adapted for use with older adults (e.g. 15 in instead of the regular eight or ten sessions, examples were made more suitable for an older population, more attention to psycho-education and repeated explanation and revision of new information and newly learned coping skills). Participating therapists attended regular supervision meetings, which were led by certified supervisors for behavior therapy (P.M.G. Emmelkamp and I.J.C. Weijnen). Participants in the sertraline condition were treated by a psychiatrist or a resident-psychiatrist in eight 20-minute sessions over a period of 15 weeks. Dosage schedules for sertraline were adapted for older adults; the starter dose was lower (25 mg) and the dosage was built up more gradually than in the customary procedure (up to a minimum dose of 100 mg which had to be reached within 4 weeks and a maximum dose of 150 mg on the basis of tolerability and lack of clinical response).

Demographic and clinical characteristics

Completers, treatment refusers and treatment dropouts were compared on several demographic and clinical characteristics which were measured at baseline. Demographic characteristics include age, sex, marital status (married versus not married) and level of education (classified as low, medium or high). Perceived health was measured with a subscale of the MOS-20 (Stewart et al., 1988; Cronbach's $\alpha = .86$). Clinical variables include the presence of comorbid depression as established with the SCID 2.0, duration of illness in years and pre-test scores on the Hamilton Anxiety Rating Scale (HARS; Hamilton, 1959; Cronbach's $\alpha = .82$) and the neuroticism subscale of the Eysenck Personality Questionnaire-revised, (EPQ-R; Eysenck et al., 1968; Eysenck et al., 1985, Cronbach's $\alpha = .78$).

Data analyses

Wait-list participants were excluded from analyses of attrition, but not from analyses involving the type of referral. We hypothesized that different factors would be involved in refusal or dropout from a psychopharmacological treatment as opposed to a psychological intervention. Therefore, the attrition analyses were performed separately for each treatment modality. Treatment dropouts and treatment refusers were compared to completers on all relevant demographic and clinical variables measured at baseline in two separate series of analyses using χ^2 tests and t tests. Recruited and clinically referred participants were compared on the same variables using χ^2 tests and t tests.

Results

Number of sessions

For CBT dropouts, the number of sessions attended ranged from one to seven (out of a total number of 15 sessions). For sertraline dropouts, the number of sessions attended ranged from one to three (out of a total number of eight sessions).

Characteristics of dropouts and refusers versus completers

Dropouts and refusers were compared to completers on all relevant pre-treatment characteristics using separate χ^2 tests and t tests for each treatment condition.

CBT dropouts and refusers

Treatment dropouts were not significantly different from completers with respect to age, distribution of sex, marital status, education and perceived health (see table 1; next page). However, CBT dropouts had a shorter duration of illness (mean duration 12.9 versus 27.9 years; $t(36) = 2.33$, $p < .05$) than CBT completers. Also, pre-test scores on the Neuroticism subscale of the EPQ-R ($t(35) = -3.87$, $p < .01$) were significantly higher in CBT dropouts than in CBT completers and CBT dropouts had a higher rate of comorbid depression (44.4% versus 10.0%; $\chi^2(1) = 5.58$, $p < .05$).

Similarly, CBT refusers had a shorter duration of illness (mean duration 6.1 versus 27.9 years; $t(31)=3.53$, $p<.01$) than CBT completers. However, CBT refusers did not differ from CBT completers on any measure of illness severity or the presence of comorbid depression as measured at baseline.

Table 1. Distribution of pre-test characteristics between completers, refusers and dropouts in CBT

Variable		CBT (n=42)		
		Completers (n=30)	Refusers (n=3)	Dropouts (n=9)
Age	M (SD)	70.60 (6.52)	73.67 (9.02)	70.11 (6.60)
Female	n (%)	21 (70.0)	3 (100.0)	7 (77.8)
Married	n (%)	17 (56.7)	2 (66.7)	4(44.4)
Education	M (SD)	1.87 (.90)	1.67 (1.16)	2.11 (.93)
Perceived health	M (SD)	15.63 (5.54)	20.90 (4.90)	11.47 (4.84)
Duration of illness (yrs)	M (SD)	27.85 (25.20)	6.06 (7.14)**	12.88 (12.65)*
Comorbid depression	n (%)	3(10.0)	0 (0)	4(44.4)*
Anxiety score (HARS)	M (SD)	14.48 (8.00)	14.33 (4.93)	19.75 (6.14)
Neuroticism (EPQ-R)	M (SD)	7.37 (3.32)	6.67 (4.16)	10.56 (1.59)**

*Significant χ^2 or t test of refusers or dropouts versus completers at $p<.05$ level

** Significant χ^2 or t test of refusers or dropouts versus completers at $p<.01$ level

Sertraline dropouts and refusers

Table 2 (next page) shows that none of the sertraline dropouts suffered from a comorbid depression, whereas 44% of sertraline completers suffered from a comorbid depression ($\chi^2 = 6.75$, $p<.01$). Sertraline dropouts did not differ from completers on any of the other clinical or demographic variables. No significant differences were found between sertraline refusers and sertraline completers on any of the variables. However, as can be seen in table 2, sertraline refusers were similar to sertraline dropouts with respect to the absence of comorbid depression.

Table 2. Distribution of pre-test characteristics between completers, refusers and dropouts in the sertraline condition

Variable		Sertraline (n=29)		
		Completers (n=18)	Refusers (n=4)	Dropouts (n=7)
Age	M (SD)	69.72 (5.92)	70.75 (1.89)	69.43 (6.24)
Female	n (%)	13 (72.2)	4 (100.0)	5 (71.4)
Married	n (%)	13 (76.5)	2 (50.0)	3 (42.9)
Education	M (SD)	1.94 (.80)	2.00 (1.16)	1.43 (.54)
Perceived health	M (SD)	13.69 (4.81)	10.99 (1.41)	16.52 (4.11)
Duration of illness (yrs)	M (SD)	31.79 (23.42)	22.63 (26.05)	29.29 (22.46)
Comorbid depression	n (%)	8 (44.4)	0 (0)	0 (0)*
Anxiety score (HARS)	M (SD)	18.32 (8.20)	14.67 (.58)	19.56 (9.32)
Neuroticism (EPQ-R)	M (SD)	9.27 (2.40)	9.33 (1.53)	8.33 (.82)

*Significant χ^2 or t test of refusers or dropouts versus completers at $p < .05$ level

Characteristics of recruited versus clinically referred participants

There was a significant difference in the distribution of sex between recruited and referred participants, with more males in the recruited group versus the referred group (see table 3 on the next page: 35.3% versus 12.1%; $\chi^2(1) = 5.57$, $p < .05$). Recruited participants were also more educated than clinically referred participants ($t(82) = -2.94$, $p < .01$). Perceived health was higher ($t(71) = -2.89$, $p < .01$) and neuroticism ($t(73) = 2.39$, $p < .05$) and anxiety scores ($t(79) = 5.12$, $p < .001$) were lower in recruited participants. Rates of comorbid depression (11.8% versus 33.3%; $\chi^2(1) = 5.77$, $p < .05$) were significantly lower in recruited participants than in clinically referred participants.

Table 3. Distribution of pre-test characteristics between
recruited and clinically referred participants

Variable		Recruited (n=51)	Clinically referred (n=33)
Age	M (SD)	69.61 (6.42)	70.09 (5.94)
Female	n (%)	33 (64.7)	29 (87.9)*
Married	n (%)	30 (58.8)	17 (53.1)
Education	M (SD)	2.08 (.85)	1.55 (.75)**
Perceived health	M (SD)	15.86 (5.11)	12.32 (4.80)**
Duration of symptoms (yrs)	M (SD)	27.08 (22.54)	24.61 (25.27)
Comorbid depression	n (%)	6 (11.8)	11 (33.3)*
Anxiety score (HARS)	M (SD)	13.67 (5.96)	21.86 (8.41)**
Neuroticism (EPQ-R)	M (SD)	7.74 (2.64)	9.31 (3.02)*

*Significant χ^2 or t test at $p < .05$ level

** Significant χ^2 or t test at $p < .01$ level

Discussion

Attrition

The present study is the first to systematically study differences in variables related to attrition in CBT versus variables related to attrition in pharmacological treatment (sertraline) for late-life anxiety disorders. Our most salient finding pertaining to this subject is that CBT dropouts seemed to suffer from higher rates of comorbid depression and showed higher trait anxiety (reflected in higher neuroticism scores) than CBT completers, whilst in contrast, sertraline dropouts showed lower rates of comorbid depression and did not differ from sertraline completers on neuroticism scores. In fact, none of the sertraline dropouts suffered from a comorbid depression compared to 44% of sertraline completers. These findings suggest that SSRIs might be more acceptable to anxious older adults with comorbid depression, whilst CBT may be more acceptable to anxious older adults low in neuroticism who do not suffer from such comorbidity. Our research group has also found neuroticism to be related to a persistent long-term outcome of late-life anxiety (see chapter 3) and to an unsuccessful treatment outcome of CBT for late-life anxiety (see chapter 5).

Apparently, anxious older adults high in neuroticism constitute a group that is particularly difficult to treat.

The fact that our results suggest that those with higher trait anxiety and a higher rate of comorbid depression tend to drop out of CBT prematurely bears several consequences, not only for the practice of treatment for late-life anxiety disorders, but also for the interpretation of treatment studies (especially since comorbid depression is highly prevalent in late-life anxiety (van Balkom et al., 2000)).

Contrary to suggestions that poor health might be an obstacle to the acceptability of both CBT (Stanley et al., 2003) and pharmacological interventions (Nordhus et al., 2003; Hersen et al., 1992) for late-life anxiety, we did not find perceived health to be related to treatment dropout or refusal in either treatment condition. However, findings pertaining to this subject are inconclusive as we failed to take into account other possibly more objective health related variables (e.g. number and nature of chronic illnesses) and our sample size was relatively small.

On a different note, we found that both CBT dropouts and refusers had a shorter duration of illness (mean duration 12.9 and 6.1 years respectively versus 27.9 years) than CBT completers. This finding runs contrary to the frequently voiced clinical impression that a long duration of illness in older adults might lead them to be less motivated for treatment.

Interestingly, refusal and dropout were not found to be related to the same variables, apart from illness duration in those randomized to CBT. In fact, in some respects treatment refusers seem to be more comparable to treatment completers than to treatment dropouts. CBT refusers did not differ from completers on rates of comorbid depression or neuroticism. Maybe those who refuse CBT after randomisation tend to do so simply because they do not agree with this choice of treatment, while those who end CBT prematurely tend to do so because they find it too straining. However, CBT refusers constituted a very small subsample in the present study ($n=3$) and studies investigating larger samples are needed to confirm these findings.

Characteristics of recruited participants versus referred mental health care patients

Although some studies have examined possible recruitment biases in treatment studies in mixed-age populations, ours was the first to study variables related to recruitment strategy in the treatment of late-life anxiety disorders. Media recruitment is frequently employed in this type of research, since older adults with anxiety disorders do not tend to seek specialized treatment for psychological symptoms and are seldomly referred to mental health care centres. In the treatment study by our research group (see chapter 4), participants were both actively recruited and clinically referred, making it possible to study differences between both groups. Recruited participants were found to be less severely impaired in several respects; with regard to initial severity of anxiety (as measured with the HARS), neuroticism, rates of comorbid depression and perceived health. Furthermore, recruited participants generally had a higher level of education than clinically referred participants. These results imply that findings from treatment studies of late-life anxiety might be based on a select population of anxious older adults who are relatively healthy, have relatively mild symptoms and are relatively well educated (Stanley et al., 2003b). Alternatively, one could claim that anxiety in older adults only leads to appropriate referral when symptoms are very severe. It would be interesting in this respect to compare illness severity between older and younger anxious adults who are presented to mental health care settings.

On a different note, the fact that there were more males among the recruited group than among the clinically referred group suggests that media recruitment might be an effective way to lower the threshold for older men to enter therapy.

Recommendations and conclusions

Treatment trials of late-life anxiety that have been conducted in the last ten years focus on media recruited populations, which may lead to a selection bias of relatively healthy subjects (both physically and mentally), who actually might not need such an

intensive and time-consuming intervention. This may also partly explain why studies of this kind tend to find lower effect sizes and higher attrition rates than those found in similar studies with mixed-age populations. Also, the threshold for a psychological intervention at a mental health care centre appears to be very high for anxious older adults. We may need to present treatment in other, more neutral settings, and in more neutral terminology (e.g. 'tension' in stead of 'anxiety', 'courses' in stead of 'therapy'; Wetherell et al., 2001).

Our results also suggest that SSRIs may be the treatment of choice for anxious older adults with comorbid depressive symptoms. However, older adults tend to be reluctant to take medication for psychological symptoms and it is vital that patients are closely informed and monitored by their physician, in order to eliminate prejudice and increase treatment adherence (Wetherell & Unutzer, 2003b). Consultation from a psychiatrist preceding the administration and monitoring of SSRIs by the general practitioner would be advisable.

Psychological interventions might be more appropriate and acceptable to older adults low in neuroticism and without a comorbid depression. The question we are faced with is whether CBT is the psychological intervention of choice for this particular group and whether this treatment may not be too time-consuming, complicated and straining for those with relatively mild symptoms. Short-term primary care interventions (based on behavioural techniques with less focus on complicated cognitive techniques) may constitute an effective and efficient psychological treatment which is more acceptable to this particular group. Future research efforts in the field of late-life anxiety treatments might do well to focus on comparative trials of such interventions versus pharmacological treatment with SSRIs monitored by the general practitioner.

In interpreting the results of the present study, it is important to take into account that analyses were performed on a relatively small study sample, increasing the risk of chance-findings. Studies involving larger samples (for example by performing a meta-analysis of attrition and recruitment in the available treatment studies of late-life anxiety to date) are needed to confirm our findings.

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Chapter 7



General discussion.

Moving toward a tailored treatment for anxiety in late life

Preface

The present thesis originated from the notion described in chapter 1, that 1) anxiety in late life is an important problem that merits separate study; and 2) the treatment of late-life anxiety is a feasible enterprise which can be achieved with roughly the same treatments that are successfully applied to younger populations.

In the course of our investigations, some of our assumptions have been confirmed, while others have been severely tested and modified in the process. In the present chapter, findings from the studies described in chapter 2 through chapter 6 are integrated and discussed. We specifically address the consequences of our findings for the assumptions with which we entered our investigations. A critical appraisal is given of the extent to which our endeavors contribute to the development of a tailored treatment of anxiety in late life. Attention is also paid to the methodological limitations of our studies and the implications of our findings for clinical practice. Finally, we provide specific recommendations for further research efforts that are needed to complete the journey toward a tailored treatment for late-life anxiety disorders.

Implications of the main findings of the present thesis

Cues for the existence of a specific age-related phenomenology of late-life anxiety

One of the main obstacles in providing adequate treatment to anxious older adults is the fact that anxiety is often not appropriately identified in late life. We hypothesized that differences in the phenomenology of anxiety between younger and older adults might partly be accountable for this problem, and therefore we conducted a study in

the general population that investigated this issue. A new questionnaire, the Senior Anxiety Scale (SAS), was specifically constructed to measure those cognitive contents of worry that we felt might differentiate older adults from their younger counterparts. Our findings implied that older adults tend to be more afraid than both young and middle-aged adults of possible physical and mental decline, the loss of autonomy and of life-threatening situations, such as criminal assault and death. These findings can probably be attributed to the fact that late life is a life phase that is typically related to a high rate of physical and mental decline and older adults are more often confronted with death and decline in their direct environment than young adults. The challenge in late life is not to let these fears become so overwhelming that the quality of life is more impaired by fears than by the reality of physical or mental decline.

Interpretation of our findings are limited by the fact that we had no data on actual physical or mental health of our sample, which makes it impossible to determine whether the higher rate of worry about these topics in the older sample may be solely interpreted as realistic. Our clinical impression is that older adults tend to overestimate certain risks, such as the risk of (for example) mental decline and the possibility that they might be admitted to a nursing home in the future. Our findings stress the importance of specific inquiry into the fear of physical and mental decline and life-threatening situations when diagnosing an older adult referred to mental health care.

Interestingly, we also found similarities on certain factors that we hypothesized would be different in older adults. The SAS incorporated items referring to worries about financial problems and worries about social isolation and disapproval because we expected older adults to score higher on these items than younger adults. This was not found to be the case. In fact, young and middle-aged adults seemed to show greater concern with regard to financial issues than older adults. Although we did find several age-related differences with regard to feared stimuli on the FSS, these differences seemed to have an onset in middle-aged adulthood rather than in late life. The only clear distinction between middle-aged and older adults we found was a

greater fear of sex and aggression in older adults, which is partly related to the greater fear of life-threatening situations found on the SAS. These results clearly stress the importance of testing our clinical impressions with regard to age-related fears in empirical studies.

Prediction of the long-term outcome of late-life anxiety disorders

In order to establish whether anxiety disorders have a similar tendency to show a persistent long-term outcome in late life as has been established in younger populations (Angst et al., 1991), chapter 3 reports on the outcome of anxiety disorders in a cohort of anxious older adults after a follow-up period of six years. Although 23% of our sample met criteria for an anxiety disorder and a further 47% met criteria for sub-clinical anxiety at six-year follow-up, we also found that a relatively high proportion (31%) of our sample met criteria for full remission at six-year follow-up. If we may conclude that approximately one third of our target population recovers spontaneously, the question is raised which patients are at risk for a persistent outcome and should therefore be the focus of intervention programs to prevent chronicity.

Results described in chapter 3 indicate that those high in neuroticism are at greater risk for persistence of anxiety. Interestingly, neuroticism is also found to be strongly predictive of an unsuccessful long-term outcome of CBT for late-life anxiety disorders in chapter 5 and is found to be related to early termination of CBT for late-life anxiety disorders in chapter 6. We also established that the meaning of neuroticism for long-term outcome can not be construed as a reflection of initial severity of anxiety symptoms. Neuroticism is generally regarded as a personality trait, reflecting negative affectivity (Clarke et al., 1982). However, as neuroticism was measured by self-report questionnaires (the DPV; Luteijn et al., 1985) in chapter 3 and the EPQ-R (Eysenck et al., 1968; Eysenck et al., 1985) in chapter 5 and chapter 6, high neuroticism scores may also reflect the tendency to perceive oneself as a generally nervous and unstable person, i.e. the tendency to perceive one's symptoms

as an unchangeable character trait rather than as something that may be cured. To illustrate, example items of the EPQ-R include 'Do you regard yourself as a nervous person' and 'do you regard yourself as a worrisome person'. As described in chapter 1, our clinical impression is that older adults tend to regard their symptoms as an unchangeable part of their personality, especially when these symptoms have an onset in early adulthood and have never been adequately treated. This disbelief in the possibility of change may hinder both spontaneous remission as well as the effective psychological treatment of anxiety in late life. High neuroticism scores do not seem to have any implications for the effectiveness of pharmacological treatment of late-life anxiety with an SSRI (see chapter 5).

The treatment of anxiety disorders in older adults

As described in chapter 1, the most common treatment of late-life anxiety disorders consisted of the prescription of benzodiazepines by the general practitioner. Findings described in chapter 3 imply that benzodiazepine use is still abundant among older adults with an anxiety disorder, while the use of SSRIs and mental health care facilities remains low, despite efforts made in recent years to enhance appropriate referral and treatment of late-life anxiety. Special interventions to aid the discontinuation of benzodiazepines in older adults may be necessary. A recent publication on long-term benzodiazepine use in a mixed-age population (mean age 63.6 years) shows positive results of an intervention consisting of a letter sent by the general practitioner containing the advice to gradually discontinue benzodiazepine use (Gorgels et al., 2005). This letter was followed by a written invitation to arrange an appointment with the general practitioner to evaluate the actual use of benzodiazepines.

However, in older adults with an anxiety disorder, merely tapering off benzodiazepine use without offering a better alternative is not sufficient. In an effort to find support for alternative interventions for the treatment of anxiety in late life, chapter 4 and chapter 5 of the present thesis report on short-term and long-term

treatment outcome in the first comparative trial of CBT versus an SSRI (sertraline) for anxiety disorders in older adults. The main findings of this trial may be summarized by stating that CBT did not perform as well as expected and that sertraline might be more beneficial for the treatment of late-life anxiety than standard individual format CBT. Furthermore, our study provides added proof against the reluctance of clinicians and researchers to examine any kind of pharmacological intervention for late-life anxiety disorders. To some extent, findings regarding the effectiveness of CBT found in our RCT are in line with other late-life anxiety treatment studies, as CBT seems to produce lower effect sizes and higher attrition rates in anxious older adults than in similar younger populations (Stanley et al., 2003a; Wetherell et al., 2003a; Stanley et al., 1996). However, CBT in our study did not perform as well as has been reported in other late-life anxiety treatment trials. This might partly be attributed to the fact that we included clinically referred participants as well as recruited participants in our trial, while most other treatment trials primarily recruited their participants through media announcements (Stanley et al., 2003a; Wetherell et al., 2003a; Stanley et al., 1996). As described in chapter 6, we found that clinically referred participants were less educated and more severely impaired at baseline in several respects than recruited participants. Clinically referred participants scored higher on initial anxiety and neuroticism and had a higher rate of comorbid depression. Moreover, clinically referred participants were found to score lower on a perceived health scale.

Results with regard to the prediction of treatment outcome (see chapter 5) indicate that neuroticism and poor perceived health are predictive of less improvement after CBT in anxious older adults. Also, neuroticism and comorbid depression are found to be related to early termination of CBT (chapter 6). These findings imply that other treatment studies of late-life anxiety might overestimate the effectiveness of CBT due to a selection bias of relatively healthy subjects.

What works for whom?

When we set out our investigations for the present thesis, our aim was not merely to establish which treatment would be most effective for late-life anxiety disorders in general, but also to find indicators that might guide the preferred choice of treatment for a certain individual in clinical practice. Early termination of treatment can be regarded as a type of treatment failure (Emmelkamp et al., 1983) and in that respect, when trying to establish what works best for whom, it is important to study factors related to treatment dropout as well as factors related to a decrease in symptoms. When summarizing findings from our study on the prediction of treatment effect (chapter 5) and our study on factors related to attrition (chapter 6), it appears that CBT might be more appropriate for those that perceive themselves as fairly healthy, with low neuroticism scores and without a comorbid depression. Sertraline seems to be more appropriate for anxious older adults with a comorbid depression and greater initial severity of anxiety. The meaning of neuroticism has been addressed in a previous section of this chapter. With regard to the meaning of perceived health for the prediction of treatment effect, a recent publication on factors related to the self-perception of health sheds an interesting light on this subject. In this study, subjective health was found to be highly correlated with self-report measures of subjective well-being (life satisfaction, anxiety and depression) and the sense of coherence⁸, while correlations with objective health-related variables were insubstantial (Schneider et al., 2004). These findings imply that perceived health in older adults may be a reflection of certain coping mechanisms and psychological factors rather than an accurate measure of objective health. Therefore, we should be careful in concluding from our study that disabled or chronically ill older adults with anxiety disorders should not be referred to CBT.

⁸ The sense of coherence (SOC) is defined as a personality orientation that “expresses the extent to which a person has a pervasive, enduring feeling of confidence that 1) the stimuli deriving from one’s internal and external environments in the course of living are structured, predictable and explicable (comprehensibility), (2) resources are available to meet the demands posed by these stimuli (manageability) and (3) these demands are challenges, worthy of investment and engagement (meaningfulness). Thus, SOC should be a personality orientation that facilitates coping with the health problems and disabilities of old age, influencing subjective health perception” (Schneider et al., 2004).

Feasibility of treatment for late-life anxiety disorders

As described in chapter 6, the RCT that we conducted and other treatment studies of late-life anxiety share two common features; high attrition rates and an arduous recruitment process. Although the fact that anxious older adults are rarely seen in mental health care settings may be ascribed to a lack of appropriate diagnosis and referral as described in chapter 1, this only partly explains the difficulties that we encountered when trying to recruit and retain eligible patients for our study. Our RCT was a multi-center trial, which took place in two regions of the Netherlands: an urban region (Amsterdam) and a primarily rural region in the South of the Netherlands (Limburg). Seven mental health care centres participated in the RCT. Among patients that were clinically referred to one of these centres, we were able to include only 33 participants in the RCT over a period of 3.5 years. The other 51 participants were recruited through announcements and interviews on television, radio and in local newspapers and through information leaflets distributed among pharmacies and general practitioner's offices. Of the total sample of 84 participants, 27 participants (32%) either refused treatment immediately after randomization ($n=10$) or ended treatment prematurely ($n=17$). On the basis of available data on the prevalence of anxiety disorders in late life, we set out to include 150 participants, but despite all our efforts we were not able to reach these numbers.

How do we explain the discrepancy between available data on the prevalence and impact of late-life anxiety and the apparent reluctance of anxious older adults to enter into a specialized treatment in a mental health care setting? A frequently heard explanation is that older adults often suffer from physical difficulties that hinder the frequent visits to a mental health care setting. Although this may partly explain the discrepancy, in our own clinical experience and the numerous phone calls that we answered in response to our recruitment efforts, this was not an explanation that we encountered on a regular basis. Among those who dropped out of treatment prematurely, no-one indicated that physical limitations had anything to do with their decision (see chapters 4 and 6). Furthermore, treatment dropout was not found to be

related to perceived health in either treatment condition of our RCT (see chapter 6). Therefore, we have come to believe that other factors contribute to this phenomenon.

As described in chapter 1, older adults may tend to interpret anxiety symptoms as signs of physical illness. For example, some patients who were referred to our RCT claimed not to suffer from panic attacks even though they fit all the criteria. In their minds, they just felt really sick when leaving the house, especially when taking a tram or a bus, and the thing to do when you are feeling sick, is to stay inside and rest, especially when you're older. Also, the majority of anxiety disorders in late life represent a continuation of symptoms that started in early or middle adulthood. The mean duration of anxiety symptoms in our RCT sample was 26 years (see chapter 4). Presumably due to this long duration, symptoms are often experienced as a personality trait: e.g. 'I do not suffer from anxiety, I simply am a worrisome individual and have been so all my life. Nothing can change that'. Furthermore, symptoms have often gone untreated through all these years, or the treatment received was inadequate. We frequently encountered stories of people receiving pharmacological treatments in the 1950s and 1960s comprised of enormous quantities of tranquilizers (according to today's standards), which led to addiction and a subsequent withdrawal syndrome. These people do not tend to think of mental health care professionals as experts who are able to cure them.

The reluctance encountered in anxious older adults to receive specialized treatment also implies that the treatments that we offer do not concur with their specific needs and expectations. With regard to CBT, treatment refusers and dropouts have often proclaimed that they did not ascribe to the treatment's rationale or that they found the treatment too straining. Especially the cognitive elements in CBT and the abundance of forms and homework assignments seem to breed resistance in older adults. However, older adults are also inclined to be suspicious of pharmacological treatments for psychological problems (Wetherell et al., 2003b); older adults often already use a lot of different medications and tend to be afraid of adverse effects. This fear may be particularly strong in older adults suffering from an anxiety disorder.

Modifications needed for treatment of late-life anxiety

As described in the preface of the present chapter, the concept of this thesis was born from the conviction that common treatments for anxiety disorders in younger populations would also be successful in older adults. Due to the problems we faced when recruiting and retaining patients for our RCT and the disappointing results of CBT in our trial, we have come to the conclusion that this assumption is incorrect and that in fact, modifications or even alternative interventions may be necessary in order to improve the feasibility as well as the effectiveness of treatment for late-life anxiety disorders. Until now, no systematic study has been performed to assess if and what modifications are necessary, but several options have been put forward by prominent researchers in the field of late-life anxiety and our own investigations have also provided us with some new hypotheses with regard to this issue. Modifications that have been put forward in chapter 1 of the present thesis will not be repeated here, since these modifications were incorporated in our CBT treatment protocols and have proven insufficient.

First of all, it may be necessary to provide treatments in a primary care rather than a specialized mental health care setting. Terms and settings related to psychiatry are often associated with taboo in the current generation of older adults. As mentioned in chapter 1, older adults tend to remain in primary care settings, and instead of trying to persuade them to enter into a specialized setting, it may be more appropriate to adjust our treatment effort to this fact. Also, our studies suggest that anxious older adults who might benefit most from a psychological intervention are those without a comorbid depression, with low neuroticism scores and high perceived health. This may represent a group with less illness severity that actually does not need a time-consuming, intensive and costly specialized mental health intervention. Short-term interventions based on behavioral techniques with less focus on complicated cognitive techniques may constitute a more feasible and efficient psychological intervention (see chapter 6). A recent pilot study provides some support for a short-term CBT intervention for late-life anxiety in primary care (Stanley et al., 2003b). Treatment with SSRIs also does not necessarily need to take

place in a specialized setting, although consultation from a psychiatrist preceding the administration of SSRIs by the general practitioner is advisable.

As described in the previous paragraph, forms and homework assignments that accompany a CBT intervention tend to breed resistance and tension in anxious older adults. A large proportion of the current generation of older adults has received a relatively low level of education and therefore, they may be afraid to make mistakes in the exercises. Also, the nature of the exercises (for example exposure) is often meant to raise anxiety levels and this may be a very demanding task for someone who has adopted reasonably effective avoidance strategies during the last 20 or 30 years of his life. Therefore, anxious older adults may need more assistance and reinforcement in order to improve adherence to homework assignments. A recent pilot study (Mohlman et al., 2003) compared standard CBT to an 'enhanced' CBT intervention for older adults. Patients in the enhanced condition received weekly telephone calls from the therapist in between sessions in which the therapist inquired about the homework assignments and offered to help them if necessary. Although preliminary, results suggest that the enhanced CBT protocol might lead to better results.

In light of our own findings and the fact that the superiority of CBT over other treatment methods has not been firmly established for late-life anxiety disorders (Mohlman, 2004), it seems appropriate that future research efforts will not merely focus on possible modifications of CBT, but will also examine whether other interventions may not provide a more suitable alternative for this particular group. CBT tends to focus on the present and on specific techniques to learn how to handle anxiety, disregarding the past, since the origin of anxiety is presumed to be of less importance. However, in a sense this may conflict with one of the main features and tasks of late life: to look back on your life and to evaluate what life and your own actions have brought you. The fact that CBT tends to disregard this need may result in a lack of appeal to an older population. Interventions in which these features of late life are reinforced may be more acceptable to anxious older adults. Recently, reminiscence therapy has come into focus for the treatment of late-life depression,

yielding positive results (Bohlmeijer et al., 2003) but this intervention may also be applicable to anxiety disorders. Reminiscence therapy does not focus on specific symptoms of depression or anxiety. Instead, older adults come together in a group to talk and write about how they have coped with certain issues (e.g. experiences of loss) during their life. The memories called forth by these proceedings may be used in two different ways: 1) if the memories carry a negative quality: e.g. “I have always been a weak person”, the therapist attempts to redefine memories in more positive terms. 2) Coping mechanisms that have proven effective in the person’s past are applied to current problems (Watt & Cappeliez, 2000).

Limitations of the present thesis

Methodological limitations of the studies described in the present thesis have already been extensively addressed in the previous chapters. Therefore, the present paragraph will only provide a short summary of the main limitations.

Conclusions regarding the appropriate identification and treatment of late-life anxiety disorders that can be drawn from our study on the phenomenology of anxiety in older adults described in chapter 2 are limited by the fact that we studied anxiety in a normal rather than a clinical population. Since age was a-priori classified in three different groups, it was not possible to deduct at what age the differences found in relation to feared stimuli measured by the FSS actually emerged.

Our study on the long-term outcome of anxiety disorders in the LASA-study (chapter 3) is limited by the loss of subjects for follow-up and the fact that analyses of outcome were restricted to one point in time, six years after baseline measurements. Our RCT (chapters 4 through 6) mainly suffered from small sample size and differences in sample size between treatment conditions which resulted in a lack of statistical power. The absence of a placebo condition and lack of an appropriate measure of adverse effects are important disadvantages. The heterogeneity of our sample may also be considered as a limitation, although as Nordhus and Pallesen (2003) have put forward in their systematic review of psychological interventions for

late-life anxiety: “the downside of homogeneity is that it yields a picture of patients that may be very different from their no-research counterparts, thus compromising generalization”. Finally, observer ratings in our RCT were not blind and measurement strategy relied heavily on self-report measures (three of four outcome measures), which may be problematic since older adults may tend to underreport psychological symptoms (Goderis et al., 1992). In the RCT, we found higher effect sizes for sertraline and a better long-term outcome of sertraline on anxiety symptoms as measured with the HARS (a clinician-rated instrument) and on worry symptoms (see chapters 4 and 5). Our study on attrition described in chapter 6 suggests that selective dropout of CBT participants with comorbid depression and high neuroticism scores and of sertraline participants without comorbid depression may have influenced these findings. We did not find any significant differences with regard to measures of illness severity at baseline between the active treatment conditions, either before or after attrition (chapter 4). However, we did find a significant difference in the rate of comorbid depression, and due to the lack of statistical power we cannot completely exclude the possibility that CBT completers represented a subgroup of participants with less illness severity at baseline than sertraline completers.

Recommendations for further research

With regard to establishing differences in the phenomenology of anxiety in late life, it would be interesting to replicate the study described in chapter 2 in a clinical population in order to find more cues to improve identification and treatment for late-life anxiety disorders. The long-term course of late-life anxiety should be closely examined in a longitudinal design, using measurements at regular time intervals in a larger sample of anxious older adults in order to make up for the inevitable loss of subjects. With regard to the treatment of late life anxiety, our findings call for more pharmacological treatment trials of SSRIs, using larger samples and a placebo condition, adequate measurement of adverse effects and attrition related to adverse effects. Our findings also call for the development and investigation of a tailored CBT

intervention, both with regard to setting (primary care versus mental health care) and contents (e.g. more guidance in homework assignments). Additionally, comparative trials of CBT versus SSRIs as well as alternative psychological interventions such as reminiscence therapy are needed to firmly establish the preferred choice of treatment for this group. Trials incorporating stepped-care interventions may provide more information with regard to which older adults may benefit from a short-term primary care intervention and which older adults need a more intensive intervention.

Final remarks

In conclusion, we feel that studies have confirmed the assumption that anxiety in late life is an important problem that merits separate study. The second part of our hypothesis, which stated that the treatment of late-life anxiety is a feasible enterprise which can be achieved with roughly the same treatments that are successfully applied to younger populations, has partly been revised in the process of our investigations. In order to establish a feasible and effective treatment for late-life anxiety disorders, state of the art treatments for younger adults need to be modified. Alternative psychological interventions may even be more appropriate for this specific population than CBT. Our findings with regard to the effectiveness of the pharmacological treatment of late-life anxiety with an SSRI (sertraline) are promising. However, the lack of adherence to treatment is a complicated problem in both psychological and pharmacological interventions for late-life anxiety (Wetherell et al., 2003b). More research is needed to resolve this issue.

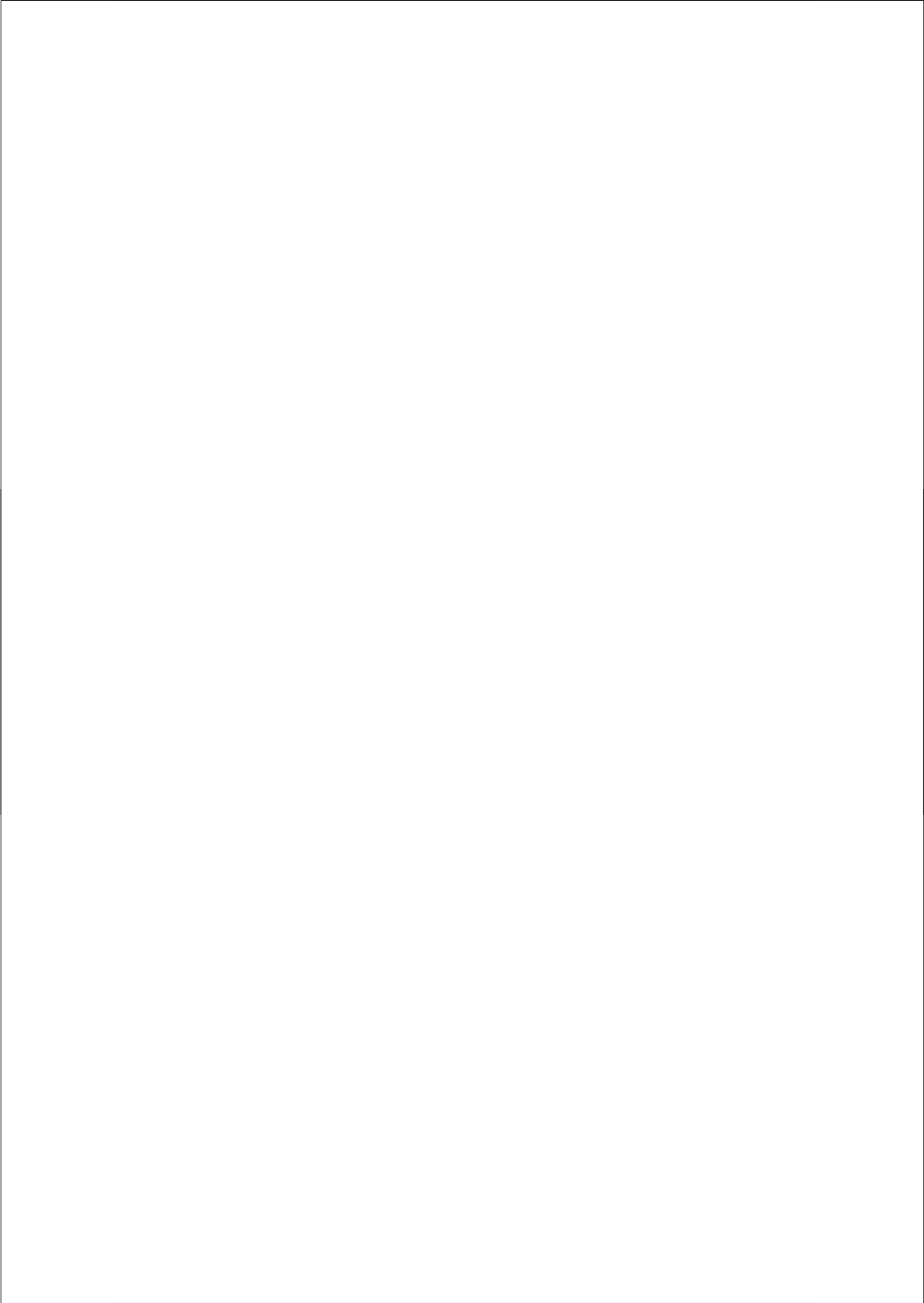
The challenge facing us now is to bridge the gap between science and clinical practice (Wetherell, Maser & van Balkom, 2005), which has been proven to be a difficult task. As has been proposed in the first chapter of the present thesis, several false notions with regard to the nature of late-life anxiety are still abundantly present in clinical practice, even though these notions have been refuted by epidemiological studies. Researchers and clinicians need to join efforts to improve the acknowledgement of

late-life anxiety as a serious problem and to continue on the road toward a tailored treatment for anxious older adults.

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Samenvatting



Angst op latere leeftijd

Op weg naar een passend behandelaanbod

Tot voor kort werd er in de klinische praktijk en in de wetenschap weinig aandacht besteed aan angststoornissen op latere leeftijd. Verschillende factoren hebben hiertoe bijgedragen.

Ouderen met een angststoornis lijken zelden in contact te komen met de geestelijke gezondheidszorg, hetgeen een van de redenen is dat er lange tijd werd aangenomen dat angststoornissen bij ouderen niet zo vaak voorkwamen, of dat angst bij ouderen beschouwd moet worden als een secundair symptoom van depressie of een voorloper van dementie. Daarnaast is er lange tijd vanuit gegaan dat angst bij ouderen weinig lijdensdruk met zich mee zou brengen. Echter zelfs bij duidelijke aanwezigheid van lijdensdruk, lijkt er al sinds jaar en dag een vaak onuitgesproken idee te bestaan, dat het überhaupt niet haalbaar en weinig zinvol is om ouderen met angstklachten adequaat te behandelen. Een lange klachtenduur en de hypothese dat ouderen te weinig flexibel zouden zijn om hun gedragspatronen nog te kunnen doorbreken worden vaak ten tonele gevoerd als redenen om maar niet meer aan een dergelijke interventie te beginnen.

Veel van de bovenstaande assumpties zijn inmiddels verworpen door recent epidemiologisch onderzoek. Angststoornissen komen meer voor bij ouderen dan welke andere psychiatrische stoornis ook, inclusief depressie, dysthymie en dementie. De prevalentie van angststoornissen bij ouderen ligt zo omstreeks de 10%, hetgeen niet erg afwijkt van de prevalentie van 12.4% die wordt aangetroffen bij jongere volwassenen. Bovendien is aangetoond dat de impact van angst op kwaliteit van leven en zorggebruik bij ouderen groot is en vergelijkbaar met de impact van depressie.

Het huidige proefschrift stelt zich ten doel een bijdrage te leveren aan de correcte identificatie, prognose en in het bijzonder de effectieve behandeling van angststoornissen bij ouderen.

De moeizame herkenning van angststoornissen bij ouderen wordt vaak aangewezen als mogelijke oorzaak voor het feit dat deze doelgroep niet adequaat behandeld wordt. Om te onderzoeken of verschillen in de fenomenologie van angst bij ouderen wellicht bijdragen aan deze moeizame herkenning, hebben we een studie uitgevoerd (beschreven in *hoofdstuk 2*), waarin jong volwassenen, volwassenen van middelbare leeftijd en oudere volwassenen met elkaar vergeleken werden met betrekking tot de stimuli die angst op roepen en de cognitieve inhouden van angst. Daartoe werd een mailsurvey afgenomen bij een representatieve steekproef van 513 proefpersonen in Nederland, die gelijk verdeeld waren in 3 leeftijdsgroepen van 1) 18-44 jaar; 2) 45-64 jaar en 3) 65 jaar en ouder. De mate van angst die door specifieke stimuli wordt opgeroepen werd gemeten met de 'Fear Survey Schedule' (FSS). Cognitieve inhouden van angst werden gemeten met de 'Worry Domains Questionnaire-Revised' (WDQ-R) en een nieuw samengesteld instrument, de 'Senior Anxiety Scale' (SAS). ANCOVA's en post-hoc Bonferroni gecorrigeerde t-toetsen werden uitgevoerd op alle totaalscores en subschaal-scores om eventuele verschillen tussen de leeftijdsgroepen vast te kunnen stellen. Alhoewel ouderen en volwassenen van middelbare leeftijd met betrekking tot gevreesde stimuli op meerdere dimensies leken te verschillen van jongere volwassenen, werden er weinig verschillen gevonden tussen ouderen en volwassenen van middelbare leeftijd op de FSS. Het enige duidelijke onderscheid tussen ouderen en de beide jongere leeftijdsgroepen op dit punt, was dat ouderen over het algemeen hoger scoorden op angst voor sex en agressie. Met behulp van een principale componenten analyse werden vier factoren geïdentificeerd op de SAS, die samen 54.7% van de totale variantie in scores verklaarden. Ouderen scoorden hoger dan jong volwassenen op twee van de vier factoren van de SAS. Een van die factoren kan geïnterpreteerd worden als de angst voor achteruitgang van lichamelijke en geestelijke gezondheid, de andere kan geïnterpreteerd worden als de angst voor levensbedreigende situaties. Met betrekking tot de WDQ bleek dat ouderen zich minder zorgen lijken te maken over

financiën dan hun jongere tegenpolen. Daarnaast werden er op de WDQ geen verschillen tussen de leeftijdsgroepen gevonden. Concluderend kan gezegd worden dat ouderen zich meer zorgen lijken te maken over mogelijke achteruitgang van hun lichamelijke en geestelijke gezondheid, de dood en de mogelijkheid het slachtoffer te worden van een misdrijf dan jong volwassenen en volwassenen met een middelbare leeftijd.

Er is tot op heden weinig bekend over het lange termijn beloop van angststoornissen bij ouderen en van de factoren die hierbij mogelijk een rol spelen. Om vast te stellen of angststoornissen bij ouderen net als angststoornissen bij jonge volwassenen over het algemeen op lange termijn een negatieve uitkomst hebben, hebben we een studie uitgevoerd waarin bij een cohort van 112 angstige ouderen (55 jaar en ouder) na een follow-up periode van 6 jaar werd vastgesteld of er sprake was van 1) een persisterende angststoornis; 2) subklinische angstklachten of; 3) een volledige remissie van de angstklachten (*hoofdstuk 3*). Daarnaast werd bestudeerd welke variabelen een voorspellende waarde hadden voor de lange termijn uitkomst van angststoornissen op latere leeftijd. Tot slot werd bekeken hoeveel van deze mensen na 6 jaar adequate hulp ontvingen, om vast te stellen of inspanningen in de afgelopen jaren om passende verwijzing van angstige ouderen te verbeteren, het beoogde effect hebben gehad. Drieëntwintig procent van onze sample voldeed na 6 jaar aan de criteria voor een angststoornis en 47% voldeed aan de criteria voor subklinische angstklachten. Een hogere score op neuroticisme bij aanvang van de studie bleek geassocieerd te zijn met de aanwezigheid van een angststoornis na 6 jaar, ook als er gecorrigeerd werd voor de ernst van angstklachten bij aanvang van de studie. Het gebruik van benzodiazepinen was hoog (43%), terwijl het gebruik van faciliteiten voor geestelijke gezondheidszorg (14%) en antidepressiva (7%) laag was bij degenen met een persisterende angststoornis. Deze resultaten impliceren dat neuroticisme ouderen kwetsbaar maakt voor een ongunstige lange-termijn uitkomst van angststoornissen. Inspanningen om ouderen met angst beter te verwijzen lijken niet het gewenste effect te hebben gesorteerd.

In antwoord op het therapeutisch nihilisme waarmee ouderen met angst ook nu nog vaak bejegend worden, is er een tegenstroming ontstaan. Deze tegenstroming stelt

zich ten doel aan te tonen dat dezelfde behandelingen die effectief zijn gebleken bij jongere volwassenen met angst, toegepast kunnen en behoren te worden bij ouderen met soortgelijke klachten. Behandelstudies die vanuit dit idee geïnitieerd zijn, hebben zich voornamelijk gericht op het vast stellen van de effectiviteit van cognitieve gedragstherapie (CGT) bij ouderen met angst, aangezien de effectiviteit van deze interventie bij jongere volwassenen ruimschoots is aangetoond. Alhoewel dergelijke studies aanleiding geven tot een gematigd positieve houding ten aanzien van de toepassing van CGT bij deze doelgroep, zijn hierbij toch enkele kritische kanttekeningen te plaatsen. Er zijn namelijk geen overtuigende bewijzen voor de superioriteit van CGT boven andere interventies voor angstklachten bij ouderen en de gevonden effectgroottes zijn beduidend lager dan de effectgroottes die worden aangetroffen bij soortgelijk onderzoek met jongere populaties. Tot op heden is er nauwelijks onderzoek gedaan naar farmacologische interventies voor angststoornissen bij ouderen. Ouderen met angst maken veelvuldig gebruik van benzodiazepinen en omdat het langdurig gebruik van deze middelen grote risico's met zich meedragen voor ouderen, wordt er in de literatuur vaak beweerd dat psychologische interventies de voorkeur verdienen. Zelfs tegen modernere middelen, zoals de serotonerge antidepressiva die bewezen effectief zijn bij jongere populaties met angst, wordt gewaarschuwd, omdat ouderen onder andere door een langzamere stofwisseling meer last zouden hebben van bijwerkingen. Om de effectiviteit van CGT bij ouderen met angst nader te onderzoeken en om vast te stellen of genoemde terughoudendheid jegens farmacologische interventies terecht is, hebben we een vergelijkende behandelstudie van CGT versus een SSRI (sertraline) uitgevoerd bij deze doelgroep. Het betrof een multi-center trial dat plaats vond in 7 GGZ-instellingen in twee verschillende regio's van Nederland; Amsterdam en omstreken en Limburg. Vierentachtig patiënten van 60 jaar en ouder met een gegeneraliseerde angststoornis, paniekstoornis, agorafobie of sociale fobie als hoofddiagnose werden at random toegewezen aan een van de volgende drie condities: CGT, sertraline of een wachtlijst controlegroep. Primaire uitkomstmaten (angst) en secundaire uitkomstmaten (piekeren en depressieve symptomen) werden afgenomen op vier verschillende tijdstippen: voorafgaand aan de behandeling, een

week na het afsluiten van de behandeling, drie maanden na afsluiten van de behandeling en een jaar na afsluiten van de behandeling. *Hoofdstuk 4* beschrijft de hoofdbevindingen van deze trial, terwijl *hoofdstuk 5* zich richt op de lange termijn effecten van beide behandelingen. Daarnaast wordt in *hoofdstuk 5* verslag gedaan van een studie naar differentiële predictoren voor het effect van beide behandelingen.

Hoofdstuk 4. De uitval van proefpersonen was in beide behandelcondities relatief groot. Daardoor zijn onze bevindingen gebaseerd op een relatief kleine sample van 'completers' ($n=52$). Hoewel zowel CGT als sertraline een significante verbetering in angst, piekeren en depressieve symptomen tot gevolg hadden, gingen deelnemers in de sertraline groep meer vooruit met betrekking tot piekeren dan deelnemers in de CGT groep. Effectgroottes voor CGT waren klein tot middelgroot, zowel vlak na de behandeling (gemiddelde $d=.42$) als na een follow-up van 3 maanden (gemiddelde $d=.35$). Effectgroottes voor sertraline daarentegen waren groot te noemen, (gemiddelde $d(\text{nameting})=.94$ en gemiddelde $d(\text{follow-up})=1.02$). De wachtlijst conditie vertoonde geen beduidende verbetering of verslechtering van klachten (gemiddelde $d(\text{nameting})=.03$).

In *hoofdstuk 5* worden onder andere de lange termijn uitkomsten van de behandelstudie beschreven. Na een follow-up van 1 jaar blijken deelnemers in de sertraline groep meer vooruit gegaan te zijn op angst (gemeten met de HARS) en piekeren (gemeten met de WDQ) dan deelnemers in de CGT conditie. Om vast te stellen welke factoren bepalen of een deelnemer gunstig reageert op een van beide behandelingen werd door middel van een regressie-analyse op residual gain scores bestudeerd of er een associatie is tussen leeftijd, opleiding, duur van de klachten, angstsymptomen, depressieve symptomen, neuroticisme en gezondheid bij aanvang van de behandeling enerzijds en de afname van klachten tussen voor en nameting en tussen de voormeting en een follow-up van 1 jaar anderzijds. Een geringere inschatting van de eigen gezondheid, de aanwezigheid van depressieve symptomen en een hoge score op neuroticisme bleek voorspellend te zijn voor een slechter behandelresultaat in de CGT groep. De sterkste voorspeller voor een slecht behandelresultaat op korte termijn na CGT was een geringe inschatting van de eigen

gezondheid, hetgeen 40% van de variantie in scores verklaarde. De sterkste predictor voor een slecht behandelresultaat op lange termijn in de CGT groep was neuroticisme, hetgeen bij de follow-up 20% van de variantie in residual gain scores verklaarde. In de sertraline groep bleek een hogere angstscore bij aanvang voorspellend te zijn voor een grotere afname van klachten op korte termijn. Angstscore bij aanvang verklaarde 41% van de variantie in residual gain scores bij de nameting. Er werden geen significante predictoren voor lange termijn effecten gevonden in de sertraline groep.

Concluderend kan gezegd worden dat onze bevindingen suggereren dat sertraline een effectievere behandeling zou kunnen zijn dan CGT voor ouderen met een angststoornis, althans wanneer CGT wordt aangeboden in een individuele setting met minimale aanpassingen voor ouderen. Een geringe inschatting van de eigen gezondheid en neuroticisme bleken voorspellend te zijn voor minder verbetering ten gevolge van CGT. Ernstigere angstklachten bleken voorspellend te zijn voor een grotere verbetering op korte termijn bij een behandeling met sertraline.

De werving van proefpersonen voor behandelstudies naar angst bij ouderen is uiterst moeizaam gebleken. Deze werving komt veelal tot stand door middel van de verspreiding van advertenties en interviews in de media. Daarnaast worden de beschikbare behandelstudies naar angst bij ouderen gekarakteriseerd door een hoge uitval van proefpersonen. Het is belangrijk om hier aandacht aan te besteden bij het evalueren van de effectiviteit van een bepaalde interventie, aangezien het vroegtijdig staken van een behandeling opgevat kan worden als een falen van die behandeling. De actieve werving en de hoge uitval van proefpersonen kan bovendien een bias van de onderzoeksresultaten tot gevolg hebben. Mensen die een behandeling vroegtijdig staken blijken vaak op verschillende factoren te verschillen van mensen die de behandeling wel afmaken. Mensen die actief geworven worden voor onderzoek via de media wijken vaak af van mensen die zichzelf aanmelden of die verwezen worden naar een instelling voor geestelijke gezondheidszorg.

In *hoofdstuk 6* wordt een studie gerapporteerd waarin nader werd onderzocht of er verschillen waren tussen weigeraars, drop-outs en completers in beide

behandelcondities van de door ons uitgevoerde trial. Ook wordt in dit hoofdstuk beschreven in hoeverre deelnemers die actief waren geworven voor het onderzoek verschilden van deelnemers die werden verwezen naar een instelling voor geestelijke gezondheidszorg.

Drop-outs in de CGT conditie bleken een hogere score te hebben op neuroticisme en zij hadden vaker een comorbide depressie bij aanvang van de studie dan CGT deelnemers die de behandeling afmaakten. Drop-outs in de sertraline conditie hadden juist minder vaak een comorbide depressie bij aanvang dan sertraline deelnemers die de behandeling afmaakten. Deelnemers die actief geworven waren via radio, tv, krant of foldermateriaal bleken hoger opgeleid te zijn en minder ernstige klachten te hebben (zowel lichamelijk als psychisch) dan deelnemers die verwezen waren naar een van de aan de trial deelnemende GGZ-instellingen. Concluderend kan gezegd worden dat de werving van deelnemers uit de algemene bevolking wellicht leidt tot een selectie van relatief gezonde proefpersonen voor behandelstudies naar angst bij ouderen. SSRI's zijn wellicht meer acceptabel voor angstige ouderen met een comorbide depressie terwijl CGT een meer passende interventie kan zijn voor angstige ouderen zonder comorbide depressie en een lage score op neuroticisme.

In *hoofdstuk 7* worden de belangrijkste bevindingen van bovenstaande studies geïntegreerd en bediscussieerd. In dit hoofdstuk wordt onder andere expliciet aandacht geschonken aan de betekenis van neuroticisme in onze studie, de haalbaarheid van psychologische en farmacologische interventies van angst bij ouderen en aan de vraag of en zo ja, welke aanpassingen er nodig zijn voor de adequate toepassing van CGT op een oudere populatie.

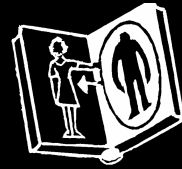
Ons onderzoek heeft naar onze mening voldoende aangetoond dat de aanname, dat angst bij ouderen een belangrijk probleem is dat aparte aandacht verdient in de wetenschap en de praktijk, juist is. Het tweede deel van onze hypothese bij aanvang van dit promotietraject, dat de behandeling van angst bij ouderen een haalbare onderneming is waarvoor in grote lijnen de bij jongere volwassenen effectief gebleken behandelingen toepasbaar zijn, is deels herzien naar aanleiding van onze

bevindingen. Om ervoor te zorgen dat de behandeling van angst bij ouderen een haalbare en effectieve onderneming wordt, moeten state of the art behandelingen voor angststoornissen op een meer ingrijpende wijze worden aangepast voor het gebruik bij een oudere doelgroep. Onze bevindingen ten aanzien van de effectiviteit van de behandeling van angst bij ouderen met een SSRI zijn veelbelovend. Het gebrek aan therapietrouw vormt echter bij zowel psychologische als farmacologische interventies een gecompliceerd probleem. Er is meer onderzoek nodig om voor deze vraagstukken een bevredigende oplossing te vinden.

De uitdaging die nu voor ons ligt, is te zorgen dat de kloof tussen wetenschap en klinische praktijk overbrugd wordt. Veel van de inmiddels door wetenschappelijk onderzoek weerlegde assumpties ten aanzien van de aard van angst op latere leeftijd zijn nog steeds volop in zwang in de klinische praktijk. Onderzoekers en klinici moeten hun krachten bundelen om de herkenning en vooral de erkenning van angst bij ouderen als serieus probleem te bewerkstelligen en om de ingeslagen weg naar een passend behandel aanbod voor angstige ouderen te vervolgen.



Dankwoord



Dit proefschrift is opgedragen aan mijn opa, Bach Schuurmans, en zijn motto: 'Mens, durf te leven'. Hij was zo'n warme en levenslustige persoonlijkheid dat ik lange tijd wilde geloven dat Magere Hein aan hem voorbij zou gaan. Tegen alle wetten der rechtvaardigheid in stierf hij natuurlijk toch, in 2001, het jaar dat ik aan dit promotie onderzoek begon. Een liedjeszanger die afgelopen jaar overleed was echter van mening dat je pas dood bent, als men je is vergeten. Ik heb geprobeerd de herinnering aan mijn opa in meerdere aspecten van mijn promotie en proefschrift terug te laten komen.

De weg naar een proefschrift is lang en begint eigenlijk bij de liefde voor een vak. Op die weg zijn er veel mensen geweest die mij op verschillende manieren hebben geholpen.

Alan Davies, die mij voor het eerst liet kennis maken met de psychologie. Ik was meteen verkocht. Pieter de Beurs en Theo Hoytink. Inspirerende docenten aan de VU. Arnoud van Loon, mijn stagebegeleider op de Valeriuskliniek, die door mijn onzekerheid heen prikte en me aanspoorde als ik dacht dat ik het niet kon.

Christine van Boeijen, Patricia van Oppen, Ton van Balkom, Loes Marquenie en Annemiek Schadé, die mij een kans gaven door mij aan te nemen als onderzoeksassistent en van wie ik heb kunnen afkijken hoe je goed onderzoek opzet en uitvoert.

Hannie Comijs, mijn copromotor, jou als vaste begeleider te hebben bij mijn promotietraject was eigenlijk een enorme luxe. Je had altijd tijd voor me, mijn mailtjes werden altijd bijna direct beantwoord (en dat waren er soms meerdere op een dag), je had waardevolle input bij de moeizame werving en je becommentarieerde mijn stukken zeer gedegen en gedetailleerd. En bovendien waren onze begeleidingsgesprekken ook altijd zo gezellig, ik mis je nu echt.

Richard van Dyck en Paul Emmelkamp. Jullie vulden elkaar goed aan als promotoren en hebben beiden een onmisbare bijdrage geleverd aan dit proefschrift. Dank voor de snelheid waarmee jullie de door mij ingestuurde stukken

becommentarieerden (met name in de eindfase van mijn promotietraject, toen ik jullie bijna iedere week iets stuurde dat om een reactie vroeg!) en voor jullie waardevolle bijdragen aan alle stukken. Richard, van jou heb ik veel geleerd over het reageren op commentaar van referenten, vooral als dit niet zo positief was. Paul, dank voor je inzet als supervisor van de gedragstherapeuten in Amsterdam en voor je voortdurende vertrouwen in de succesvolle afronding van dit project, ook in tijden dat het minder goed ging.

Patricia, jou moet ik minstens twee keer bedanken. Mijn promotietraject was zeker in de beginjaren een vaak frustrerende bezigheid, maar ik kon altijd bij jou binnen komen lopen om stoom af te blazen en om vervolgens, gewapend met jouw nuchtere adviezen, de strijd weer aan te gaan. Zonder jou weet ik echt niet of ik het wel had volgehouden en je bent dan ook met recht mijn paranima vandaag.

Ingrid Weijnen en Marcel van den Hout, die jarenlang vanuit Limburg het onderzoek dat daar plaats vond coördineerden. Zonder de samenwerking met jullie zou deze studie nooit tot een goed einde hebben kunnen komen.

Edwin de Beurs. Vooral in de beginfase heb je bij het ontwerpen van deze studie en de gebruikte behandelprotocollen een belangrijke rol gespeeld. Er was op dat vlak al veel werk verricht voordat ik bij het project betrokken raakte.

Zonder het geduld en doorzettingsvermogen van alle deelnemende behandelaars, die met een uitdagende en soms veeleisende doelgroep moesten werken, was dit project nooit van de grond gekomen. Gezien de vele instellingen die aan dit project deel hebben genomen zal ik ongetwijfeld iemand vergeten, maar ik noem in Amsterdam en omstreken: Jacomien van der Linden, Marga Kuipers, Jari Hariju, Paul Korstens, Saskia Ohlin, Jorinde van der Kloek, Peter de Ruig, Dorien Postma, Caroline Sonnenberg, Sannie Hamerlink, Eric van Exel, Kathleen Thomaes, Ethy Dorrenpaal, Willeke van Zelst. In Limburg: Mike Verkaaik, Joyce Straalman, Aimee Janssen, Hanneke Zuiderveld, Jan Oosterwijk en natuurlijk Ingrid Weijnen.

Alle deelnemende instellingen; RIAGG Midden Limburg, RIAGG Noord Limburg, RIAGG Maastricht, RIAGG Sittard, GGZ Buitenamstel, de Geestgronden en de afdelingshoofden van de desbetreffende afdelingen voor ouderen, veel dank voor de medewerking en het in ons onderzoek gestelde vertrouwen.

De patiënten die hebben deelgenomen aan de behandelstudie en het fenomenologie-onderzoek wil ik uitdrukkelijk bedanken voor hun medewerking, hun inzet en de moed die zij hebben getoond door de stap naar de hulpverlening te zetten.

Len Hillen, die aan het begin van dit project de eerste intakes in Amsterdam deed en andere gegevens verzamelde, Dagmar Vink, die data verzamelde in Limburg en Astrid Dello, die aan het eind van het project de metingen in Limburg overnam van Ingrid, veel dank voor jullie bijdrage.

Marijke van der Toolen en Anneke Hermans. Veel dank voor jullie nauwgezetheid, snelheid en inspanningen bij het opsporen van talloze artikelen.

Jan Smit, die zelf vindt dat hij helemaal geen geduld heeft voor het gezeur van andere mensen, maar ik weet wel beter.

Pim Cuijpers, Theo Hoytink en Marianne Ouwehand; dank voor de ruimte die ik heb gekregen om mijn proefschrift af te ronden en voor jullie begrip en steun bij de door slapeloze nachten soms wat moeizame start van mijn nieuwe baan op de afdeling klinische psychologie van de VU.

Bij het schrijven van dit dankwoord bemerk ik dat er veel mensen zijn die ik mijn dank wil betuigen voor dingen die, althans in directe zin, niets met het schrijven van dit proefschrift van doen hebben.

Auke en Joke. Eigenzinnige ouders maken eigenzinnige kinderen, en dat is maar goed ook. Als ik jullie opvoeding in een zin zou moeten samenvatten, dan is het denk ik; 'doe het maar zoals je het zelf wil doen, dan doe je al gewoon genoeg'. Door jullie non-conformisme en ruimdenkendheid heb ik geleerd niet snel iets raar te vinden of te veroordelen en dat komt me bij mijn werk nu erg goed van pas.

Joke en Riet, oftewel de Mobiele Oma Brigade, die files, weer en wind trotseerden om Abel en later ook Jip bij ziekte of andere noodgevallen voor ons op te vangen. Zonder jullie had dit proefschrift er gewoon nog lang niet gelegen.

Gijs. De Allerbeste Grote Broer die een Zus zich wensen kan en een van de laatste Echte Ridders. Je staat vandaag naast me op dat enge grote podium, dus mij kan niets gebeuren.

Willem en Liesbeth, mijn oudste kameraadjes. Zo lang ik jullie bij me heb raak ik nooit de weg kwijt. Willem, jou wil ik ook enorm bedanken voor al je hulp bij het scannen en bewerken van de illustraties. Liesbeth, wat heerlijk voor je dat je nu eindelijk die lange reis met Joris maakt waar je al zo lang naar uitkeek, maar wat zal ik je missen vandaag.

Sas en Noor, iets nieuwere kameraadjes. Aan jullie allebei veel dank voor alle opbeurende mails, gesprekken en attenties als ik het even niet meer zo zag zitten. Sas, zonder jou had ik het weerbarstige programma 'Word' nooit kunnen bedwingen en je hebt ook nog eens mijn hele proefschrift nagekeken op redigeerfouten!

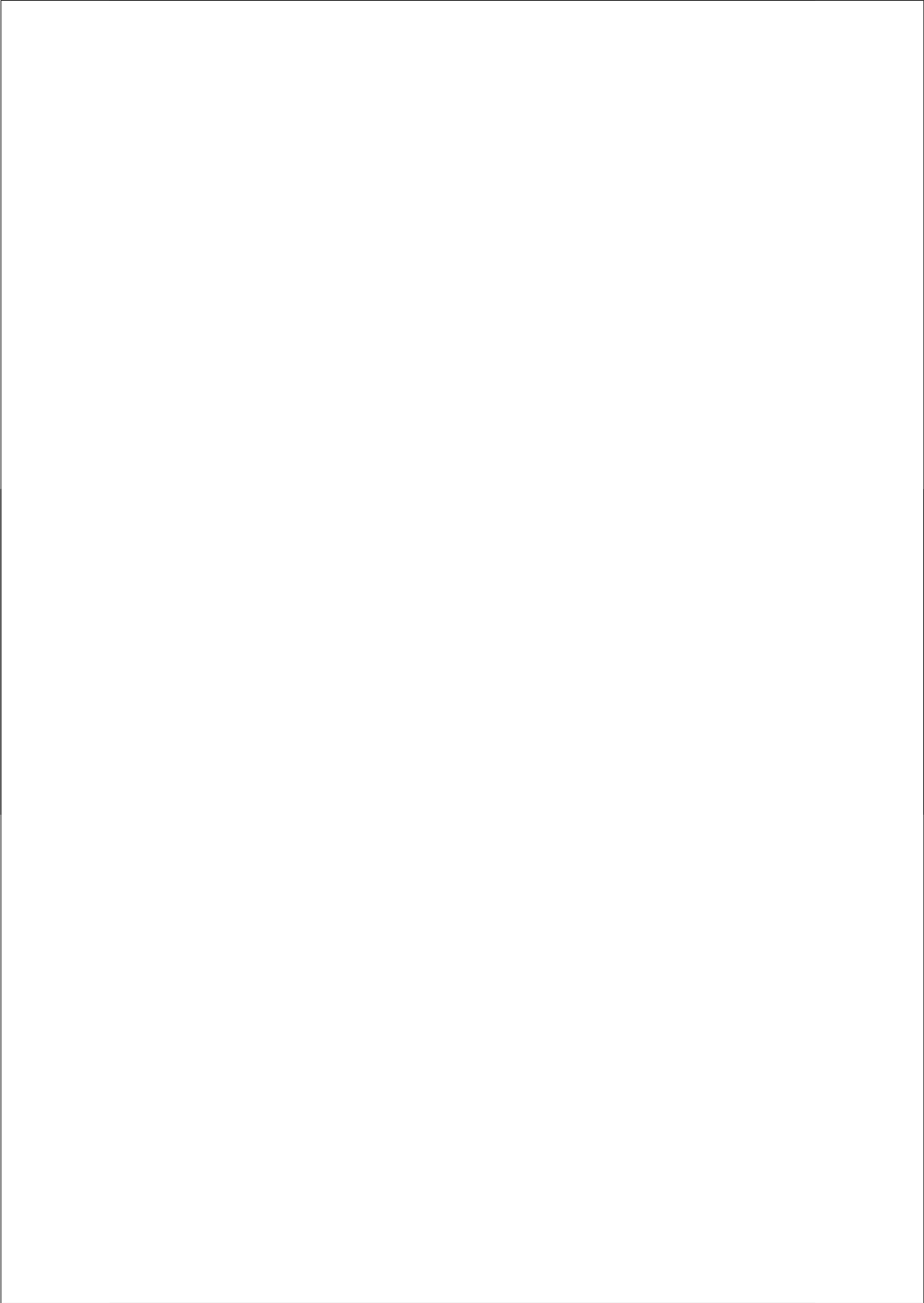
Sommige mensen markeren een keerpunt in je leven. Zonder hen zou alles anders zijn geweest. Voor mij zijn dit twee mensen, die ik omstreeks dezelfde tijd ontmoette, nu ongeveer twaalf jaar geleden: Mevrouw Martijn, Maurice.

Mevrouw Martijn, ik heb eindelijk dat boek dat steeds onder mijn bed lag maar eens weggegooid.

Maurice, twaalf jaar geleden liep je op jouw nonchalante wijze binnen bij het gezinstherapiepracticum op de VU. Met een te ruim zittende blouse en idem broek aan, je haren naar achteren gekamd en die Jack Nicholson wenkbrauwen. Nu zijn we ruim tien jaar verder en zijn we zelf een gezin geworden. Promoveren, werk en kinderen combineren kan prima, mits je iemand naast je hebt staan die ook daadwerkelijk in alle facetten van zo'n druk bestaan *naast* je gaat staan. Dat kan je als geen ander. Bedankt daarvoor. Dat drukke bestaan zorgt er soms wel voor dat we weinig tijd over houden om weer even terug te gaan naar hoe het allemaal begon;

gewoon wij met zijn tweetjes, door de stad zwalkend tot 's ochtends vroeg, omdat we allebei geen afscheid konden nemen. Maar iedere keer als we de tijd nemen en de wereld even verdwijnt, voelt alles weer net zoals toen. Ik hoop dat dat altijd zo mag blijven.

Het allerbeste en allerleukste wat me ooit is overkomen; moeder worden. Abel. Jouw enthousiasme over de gewone dagelijkse dingen ('Kijk, mamma, het stoplicht is groen! GROEN!' of 'JAAAA! wij gaan BOODSCHAPPEN doen!') is geweldig aanstekelijk. En als ik ergens pijn heb krijg ik er van jou altijd een kusje op en dan is het ook echt meteen over. Jip. Het liefste kleine vrouwtje van Nederland.



Je leeft maar heel kort, maar een enkele keer
En als je straks anders wilt, kun je niet meer
Mens, durf te leven
Vraag niet elke dag van je korte bestaan:
Hoe hebben m'n pa en m'n grootpa gedaan?
Hoe doet er m'n neef en hoe doet er m'n vrind?
En wie weet, hoe of dat nou m'n buurman weer vindt?
En - wat heeft 'Het Fatsoen' voorgeschreven?
Mens, durf te leven!

De mensen bepalen de kleur van je das
De vorm van je hoed, en de snit van je jas
En - van je leven
Ze wijzen de paadjes, waarlangs je mag gaan
En roepen 'o foei!' als je even blijft staan
Ze kiezen je toekomst en kiezen je werk
Ze zoeken een kroeg voor je uit en een kerk
En wat j'aan de armen moet geven
Mens, is dat leven?

De mensen - ze schrijven je leefregels voor
Ze geven je raad en ze roepen in koor:
Zo moet je leven!
Met die mag je omgaan, maar die is te min
Met die moet je trouwen - al heb je geen zin
En daar moet je wonen, dat eist je fatsoen
En je wordt genegeerd als je 't anders zou doen
Alsof je iets ergs had misdreven
Mens, is dat leven?

Het leven is heerlijk, het leven is mooi
Maar - vlieg uit in de lucht en kruip niet in een kooi
Mens, durf te leven

Je kop in de hoogte, je neus in de wind
En lap aan je laars hoe een ander het vindt
Hou een hart vol van warmte en van liefde in je borst
Maar wees op je vierkante meter een Vorst!

Wat je zoekt, kan geen ander je geven
Mens, durf te leven!

tekst van Jean-Louis Pissuise

